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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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T, LU, MC, NL, PT,	DK, BS, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, OAPI patent (BF, B), CF, CG, CI, CM, GA, GN, GW,	NTECH,	South San Franci	plicant (for all designated States except US): GENENTECH, INC. [USUS]; I DNA Way, South San Francisco, CA	(71) Applicant (for all designated States except US): GUNENTECH, INC. [USUS]: 1 DNA Way, South San Francisco, CA	
tant (AM, AZ, BY, KG	MD, RU, TJ, TM), European par			(continued after the drawings)	(continued a	
II, GM, KE, LS, MW	YU, ZA, ZW, ARIPO patent (G)	9 September 1998 (09.09.98)	9 Septem	60/099,602	
IT, UA, UG, US, UZ,	SG, SI, SK, SI., TJ, TM, TR, TT, UA, UG, US, UZ,		September 1998 (09.09.98	9 Septemb	60/099,598	
PL, PT, RO, RU, SD	MK, MN, MW, MX, NO, NZ.	ะ	September 1998 (09.09.98)	9 Septemb	60/099,596	
LS, LT, LU, LV, MD,	KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,	_	September 1998 (09.09.98)	9 Septemb	60/099,536	
	GB, GD, GE, GH, GM, HR, H	S	September 1998 (02.09.98)	2 Septemb	60/098,843	
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AT. AU, AZ, BA, BB	(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB	_	September 1998 (02.09.98)	. 2 Septemb	60/098,803	
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l.; Genentech, Inc., 1	(74) Agents: KRESNAK, Mark, T. et al.; Genentech, Inc.,				(30) Priority Data:	
D, William, I. [US/US , CA 94010 (US).	Monga, CA 94556 (US), WOOD, William, I. [US/US Southdown Court, Hillsborough, CA 94010 (US).	01.09.99)	1 September 1999 (01.09.99)		(22) International Filing Date:	
rlingame, CA 94010 /USI, 128 Curlisy I	[AU/US]; 19 Dwight Road, Burlingame, CA 94010 WATANALIL, Colin, K. [US/US]; 128 Curliss I	99/20111	r: PCT/US99/20111	Application Number	(21) International Application Number:	
9 March 2000 (09.0	(43) International Publication Date:	A2	C12N 15/62, 2N 5/10	C12N 15/12, C07K 14/705, C12N 15/62, C07K 16/28, C12Q 1/68, C12N 5/10	C12N 15/12, C07K 16/28,	
WO 00/12:	(11) International Publication Number:		,7:	Patent Classification	(51) International Pacent Classification 7:	
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MR. NE, SN, TD, TG). WAY GENERAL BE

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Published

Without international search report and to be republished upon receipt of that report.

(54) Title: FURTHER PRO POLYPEPTIDES AND SEQUENCES THEREOF

ОМОМЕСТИТЕСТВИВОСОМИМЕТОВОЕМПОСТВЕТЕТЕТЕМИ ВО МОМОЕТСТВЕТЕМИ В ОВСЕМЕНИЕМ В ОВСЕМЕНЕМЕМЕНЕМ В ОВСЕМЕНИЕМ В ОВСЕМЕНИЕМ В ОВСЕМЕНИЕМ В ОВСЕМЕНЕМЕМЕНЕ ndelataacaantaaccaata-dagamatic<mark>ela</mark>cciaatoratocotogogoctaatocitet Ctacettaagaacaattagogocccccctotolatacaagaacta NCACIONOMIANOCTICTYOCANTYONATTIOCOCLAROCTOADCCYODGAGATTI NETT THOSE CACCUT MIGHTON THOCHACTOC COAGE ENCHOCATOGATOETA racatragateraca acroceteragaatratereggargoscetetgargo

(57) Abstract

Membrano-bound proteins and receptor moleculer have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoalhesits, for fustance, can be employed as thempostic agents to block receptor-ligand interactions. The membrano-bound pencits can tab be employed for screening of potential peptides or mail molecule inhibitors of the relevant ecopatorilgand interaction. Efforts are being undertaken by both industry and academia to identify one coding sequences for noted proteins. Many efforts are focused on the streening of mammalian recombinant DMA illurates to identify the coding sequences for noted proteins or membrane-bound proteins. The present invention is directed to noted physpides and to nucleic not including those polypopides. Also provided herein are vectors and lost cells comprising those nucleic acid sequences, chiractic polypopides of the present invention fused to hereatle plant polypopides and to nucleic acid and the polypopides comprising the optivities of the present invention and to methods for producing the polypopides of the present invention.

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FURTHER PRO POLYPEPTIDES AND SEQUENCES THEREOF

FIELD OF THE INVENTION

The present invention relates generally to the identification and isolation of novel DNA and to the recombinant production of novel polypeptides.

BACKGROUND OF THE INVENTION

Extracellular proteins play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

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Secreted proteins have various industrial applications, including as pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at prezent, such as thrombolytic agenta, interferons, interfeukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents. Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., <u>Proc. Natl. Acad. Sci.</u> 93:7108-7113 (1996); U.S. Patern No. 5,536,637)].

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Membrane-bound proteins and receptors can play important roles in, among other things, the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by accreted polypeptides (for instance, mitogenic factors, survival factors, eytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptors kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesin molecules like selectins and integrine. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphoxylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor.

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Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesina, for instance, can be employed as theraportic agents to block receptor-ligand interactions. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are being undertaken by both industry and academia to identify new, native receptor or membrane-bound proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor or membrane-bound proteins.

PRO1560

The tetraspan family of proteins has grown to include approximately 20 known genes from various 10 species, including drosophila. The tetraspans are also known as the transmembrane 4 (TM4) superfamily and are proposed to have an organizing function in the cell membrane. Their ability to interact with other molecules and function in such diverse activities as cell adhesion, activation and differentiation, point to a role of aggregating large molecular complexes. Skubitz, et al., Linamanology, 157:3617-3626 (1996). The tetraspan group has also emerged as a set of proteins with prominent functions in Schwann cell biology. Mirsty and 15 Jessen, Curr. Optin, Neurobjol., 6(1):89-96 (1996). Tetraspans (also sometimes valled tetraspanins) are further described in Maceker, et al., EASEB, 11:428-442 (1997). Thus, members of the tetraspan family are of interest.

PRO444

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins.

Many efforts are focused on the screening of mammalian recombinant DNA lithraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO444.

PRO1018

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Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypoptide designated herein as PRO1018.

30 4. PROIZ

The primary and rate-limiting step in retinoic acid biosynthesis requires the conversion of retinol to retinal. Retinol dehydrogenase proteins are enzymes which function to recognize holo-collular retinol-binding protein as a substrate, thereby catalyzing the first step of retinoic acid biogenesis from its substrate. Various retinol dehydrogenase, genes have been cloned and characterized, wherein the products of these genes are suggested as potentially being useful for the treatment of retinitis pigmentosa, psoriasis, acne and various cancers (Chai et al., <u>J. Biol. Chem.</u> 270:28408-28412 (1995) and Chai et al., <u>Gene</u> 169:219-222 (1996)). Given the obvious importance of the retinol dehydrogenase enzymes, there is significant interest in the identification and

characterization of novel polypoptides having homology to a retinol dehydrogenase. We herein describe the identification and characterization of novel polypoptides having homology to a retinol dehydrogenase protein, designated herein as PRO1773 polypoptides.

S. PROLATI

Glycnsylation is an important mechanism for modulating the physiochemical and biological properties of proteins in a stage- and tissue-specific manner. One of the important enzymes involved in glycusylation in Succharomyces cerevisine is olpha 1,2-mannosidase, an enzyme that catalyzes the conversion of Man9GlcNAc2 to Man9GlcNAc2 during the formation of N-linked oligosaccharides. The Saccharomyces cerevisiae alpha 1,2-mannosidases and the mannosidases in general in glycusylation and the important roles played by the alpha 1,2-mannosidases and the mannosidases in general in glycoxylation and the physiochemical activity regulated by glycoxylation, there is significant interest in identifying novel polypeptides having homology to one or more mannosidases. We herein describe the identification and characterization of novel polypeptides having homology to a mannosidase protein, designated herein as PRO1477 polypeptides.

PRO1478

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Recently, a new subfamily of galactosyltransferase genes that encode type II transmembrane proteins was identified from a mouse genomic library (Hennet et al., (1998) J. Biol. Chem. 273(1):58-65) Galactosyltransferases, in general, are all of interest. Beta 1,4-galactosyltransferase is been found in two subcellular compartments where it is believed to perform two distinct function. Evans, et al., logsiants 17(3):261-268 (1995). Beta 1,4-galactosyltransferase is described as a possible transducing receptor in Dubois and Shur, Adv. Exp. Med. Biol., 376:105-114 (1995), and further reported on in Shur, Glycobiology, 1(6):563-575 (1991). Expression and function of cell surface galactosyltransferase is reported on in Shur, Blochim Biophys. Acta., 988(3):389-409 (1989). Moreover, the receptor function of galactosyltransferase during mammalian fertilization is described in Shur, Adv. Exp. Biol., 207:79-93 (1986), and the receptor function during cellular interactions is described in Shur, Mol. Cell Biochem., 61(2):143-158 (1984). Thus, it is understood that galactosyltransferases and their related proteins are of interest.

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. PROM

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30 Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted protein. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO831.

8. PRO1113

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Protein-proteininteractions thehade receptor and smigen complexes and signaling mechanisms. As more is known about the structural and functional mechanisms underlying protein-protein interactions, protein-protein

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interactions can be more easily manipulated to regulate the particular result of the protein-protein interaction.

Thus, the underlying mechanisms of protein-protein interactions are of interest to the scientific and medical community.

All proteins containing leachine-rich repeats are thought to be involved in protein-protein interactions. Leachine-rich repeats are short sequence motifs present in a number of proteins with diverse functions and cellular locations. The crystal structure of ribonuclease inhibitor protein has revealed that leache-rich repeats correspond to beta-alpha structural units. These units are arranged so that they form a parallel beta-sheet with one surface exposed to solvent, so that the protein acquires an unusual, nonglubular shape. These two features have been indicated as responsible for the protein-binding functions of proteins containing leucine-rich repeats. See, Kobe and Deisenbofer, Trends Biochem, Sci., 19(10):415-421 (Oct. 1994).

30 ટ 20 15 5 in a complex associated with the bleeding disorder Bernard-Soulier syndrome, Chlemetson, K. $I_{\cdot\cdot\cdot}$ Thromb 70 (Dec. 1996) (gonadotropin receptor involvement); Miura, Y., et al., Nippon Rinsho (Japan), 54(7):1784-1789 as in Parkinson's disease, and for diagnosis of cancer, see, Artavanistsakonas, S. and Rothberg, J. M., reported to be useful in treating neuro-degenerative diseases such as Alzheimer's disease, nerve damage such associated therapies concerned with re-growth of tissue, such as connective tissue, skin and bone; in promoting of proteins having leucine rich repeats include: Tayar, N., et al., Mol. Cell Endogrinol., (Ireland), 125(1-2):65of IGF (ALS) is also of interest in that it increases the half-life of IGF and is part of the IGF complex in vivo body growth in humans and animals; and in stimulating other growth-related processes. The acid labile autumit E. I., et al., WO9110727-A by La Jolla Cancer Research Foundation reporting that decorin binding to et al., Vouv. Rev. Fr. Hematol. (Germany), 37(4):215-222 (1995), reporting mutations in the leucine rich motif (1997). Others studies implicating leucine rich proteins in wound healing and tissue repair are De La Salle, C. ussue repair, and numor stroma formation. Iozzo, R. V., Crit. Rev. Biochem, Mol. Biol., 32(2):141-174 ordering collagen fibrils during untugeny and are involved in pathological processes such as wound healing, (July 1996) (apoptosis involvement); Harris, P. C., et al., I. Am. Soc. Nephrol., 6(4):1125-1133 (Oct. 1995) Suzuki, et al., I. Biol. Chem. (U.S.), 271(37):22522 (1996). Other studies reporting on the biological functions specifically in glial cells in the mouse brain, and has leucine rich repeats and immunoglobulin-like domains WO9210518-A1 by Yale University. Of particular interest is LIG-1, a membrane glycoprotein that is expressed function to this group of proteins is the insulin like growth factor (IGF), in that it is useful in wound-bealing and transforming growth factorf has involvement in a treatment for cancer, wound healing and scarring. Related by Haemost. (Germany), 74(1): 111-116 (July 1995), reporting that platelets have leucine rich repeats and Ruoslahti, A study has been reported on leucine-rich proteoglycans which serve as tissue organizers, orienting and Another protein which has been reported to have leucine-rich repeats is the SLIT protein which has been

9. PRO1194

(kidney disease involvement)

35 The nuclear genes PET117 and PET119 are required for the assembly of active cytochrome c oxidase in S. Cerevisiae, and therefore, are of interest. Also of interest are nucleic acids which have sequence identity with these genes. PET genes are further described in McEwen, et al., Qur. Genet., 23(1):9-14 (1993).

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10. PRO1110

The bone marrow plays many important roles in the mammal. One of those roles is to provide a source of various progenitor cells that differentiate into important cells and other components of the blood and immune systems. As such, the function of the myeloid system is of extreme interest.

We berein describe the identification and characterization of novel polypeptides having homology to myeloid upregulated protein, designated berein as PRO1110 polypeptides.

11. PRO137

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1378.

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12. PRO1481

Efforts are being undertaken by both industry and academia to identify new, native proteins. Many 15 efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel proteins. We herein describe the identification and characterization of a novel protein designated berein as PRO1481.

13. PROLISS

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There has been much interest in the identification of receptor proteins on stem cells and progenitor cells which may be involved in triggering proliferation or differentiation. A type II transmembrane protein was identified in proliferating progenitor cells in the outer perichondrial rim of the postural mandibular condyle proliferation. The investigators concluded that E25 could be a useful marker for chondro-osteogenic differentiation (Delecersnijder, et al. 1, Biol. Chem. 221(32):19475-19482 (1996)).

14. PRO14

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Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1415.

15. PRO141

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Efforts are being undertaken by both industry and academia to identify new, native secreted proteins.

Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding 35 sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated berein as PRO1411.

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PR01295

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for movel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated bettein as PRO1295.

PRO135

Enzymes such as byaluconidase, sialyltransferase, urokinase-type plasminogenactivator, plasmin, marix metalloproxelmasea, and others, play central roles in the catabolism of extracellular matrix molecules. As such, these enzymes and inhibitors thereof, may play roles in metastatic cancer and the treatment thereof. Van Aswegen and the Plessis, Med. Hypothesea, 48(5):443-447 (1997). For the foregoing reason, as well as their diversity in substrate specificity example, sialyltransferases are of particular interest. For example, a peptide of interest is the GalNAc alpha 2, 6-sallytransferases are described in Kurosawa, et al., L. Biol. Chem., 269(2):1402-1409 (1994). This peptide was constructed to be secreted, and retalacd its catalytic activity. The expressed enzyme exhibited activity toward asialomucin and asialofetuin, but not other glycoproteins tested. As sialylation is an important function, sialyltransferases such as this one, and peptides related by sequence identity, are of interest. Sialyltransferases are further described in the literature, see for example, Sjoberg, et al., L. Biol. Chem., 271(13):7450-7459 (1996). Touji, J. Biochem., 120(1):1-13 (1996) and Hardwin-Lepers, et al., Glycobiology, 5(8):741-758 (1995).

18. PRO1190

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Kang et al. reported the identification a novel cell surface glycoprotein of the lg superfamily (1,Cell biol. (1997) 138(1):203-213). Cell adhesion molecules of the lg superfamily are implicated in a wide variety of biological processes, including cell migration, growth coatrol, and numorigenesis. The Kang et al. studies suggest that loss of CDO function may play a role in oncogenesis. Accordingly, the identification of additional CDO-like molecules, and more generally, cell adhesion molecules of the lg superfamily, is of interest.

9. PRO1772

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Peptidases are enzymatic proteins that function to cleave peptide substrates either in a specific or nonspecific manner. Peptidases are generally involved in a large number of very important biological processes in
mammalian and non-mammalian organisms. Numerous different peptidase enzymes from a variety of different
mammalian and non-mammalian organisms have been both identified and characterized. The mammalian
peptidase enzymes play important roles in many different biological processes including, for example, protein
digession, zerivation, inactivation, or modulation of peptide hormone activity, and alteration of the physical
properties of proteins and enzymes.

35 In light of the important physiological roles played by poptidase enzymes, efforts are currently being undertaken by both industry and academia to identify new, native peptidase homologs. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for

novel transmembrane proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., <u>Proc. Natl. Acad. Sci., 93</u>:7108-7113 (1996); U.S. Patent No. 5,536,637)]. We betein describe the identification of novel polypeptides having bomology to various peptidase enzymes, designated herein as PRO1772 polypeptides.

20. PRO1248

Putative protein-2 (PUT-2) is a homolog of the human disease genes L1CAM, G6PD and P55 (Riboldi Tumnicliffe et al., Genome Analysis, submitteel). As such, there is inverest in identifying rovel polypeptides and encoding DNA having homology to the PUT-2 protein. We herein describe the identification and characterization of novel polypeptides having homology to PUT-2 protein, designated herein as PRO1248 polypeptides.

21. PROLITI

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Dickkopf (Dkk) is a family of secreted proteins having a high degree of homology in the cysteine-rich domains (i.e., 80-90%). Dkk-1, the first discovered member, of this family has potent head-inducgin activity on the Spemann organizer. Glinka et al., Nature 391 (6665): 357-362 (1988). The Spemann organizer of the amphibian embryo can be subdivided into two discrete activities, namely trunk organizer and head organizer. Dkk-1 has been found to be both sufficient and necessary to cause head induction in Xenopus embryos and is further a potent antagonist of Wm signaling, suggesting that the Dkk genes encode an entire family of Wm inhibitors.

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Members of the Wm gene family function in both normal development and differentiation as well as 20 in tumorigenesis. Wms are encoded by a large gene family whose members have been found in round worms, insects, carrillaginous fish, and vertebrates. Holland et al., Dev. Suppl., 125-133 (1994). Wm genes encode a family of secreted glycoproteins that modulate cell fate and behavior in embryos through activation of recopror-mediated signaling pathways.

35 ಜ 25 Varmus, H.E., Cell 69: 1073-1087 (1992)), and precocious alveolar development. Bradbury et al., Dev. Biol., mutations in mice have shown Wats to be essential for brain development (McMahon and Bradley, Cell, 62: patterning. In Drosophila, wingless (wg) encodes a Wrn-related gene (Rijszwik et al., Cell, 50: 649-657 (1987)) 170: 553-563 (1995). Moreover, constitutive expression of Wnt-4 in virgin hosts of transplanted mammary in the mammary gland can result in mammary hyperplasia and tumors, ((McMahon, supra (1992); Nusse and 174-189 (1994)), and limb bud. Parr and McMahon, Nature, 374: 350-353 (1995). Overexpression of Wats primordia for kidney (Stark et al., Nature, 372: 679-683 (1994)), tail bud (Takada et al., Genes Dev., 8: 1073-1085 (1990); Thomas and Cappechi, Nature, 346: 847-850 (1990)), and the outgrowth of embryonic required for asymmetric cell divisions. Herman and Horvitz, Development, 120: 1035-1047 (1994). Knock-out Nusse, Dev. Biol., 166: 396-414 (1994). In Caenorhabditis elegans, lin-44 encodes a Wm bomolog which is and Lawerence, Dev. Biol., 56: 227-240 (1977); Baker, Dev. Biol., 125: 96-108 (1988); Klingensmith and and wg mutations alter the pattern of embryonic ectoderm, neurogenesis, and imaginal disc ontgrowth. Morata epithelium tesuted in highly branched tissue, similar to a pregnancy-like growth pattern. Bradbury et al., Dev Studies of mutations in Wnt genes have indicated a role for Wnts in growth control and tissue

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Biol. 170: 553-563 (1995).

The Wnt/Wg signal transduction pathway plays an important role in the biological development of the organism and has been implicated in several human cancers. This pathway also includes the nume suppressor gene, APC. Mutations in the APC gene are associated with the development of oporadic and imberited forms of human coloractal cancers. For example, elevated levels of Wnt-2 have been observed in coloractal cancers. Vider, B-Z. et al., Oncogene 12: 153-158 (1996).

PR01197

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins.

Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding
to sequences for novel secreted proteins. We herein describe the identification and characterization of a novel
secreted protein designated herein as PRO1197.

ENV. 122

Insumoglobulins are anilbody molecules, the proteins that function both as receptors for antigen on the B-cell membrane and as the secreted products of the plasma cell. Like all antibody molecules, immunoglobulins perform two major functions: they bind specifically to an antigen and they participate in a limited number of biological effector functions. Therefore, new members of the lg superfamily and fragments thereof are always of interest. Molecules which act as receptors by various virtuses and those which act to regulate immune function are of particular interest. Also of particular interest are those molecules which have homology to known lg family members which act as virus receptors or regulate immune function. Thus, molecules having homology to lg superfamily members and fragments thereof (i.e., heavy and light chain fragments) are of particular interest.

We herein describe the identification and characterization of novel polypeptides having homology to an immunoglobulin heavy chain variable region protein, designated herein as PRO 1293 polypeptides.

24. PRO1380

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Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1380.

25. PRO1265

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The identification of novel secreted proteins involved in physiological and metabolic pathways is of interest because of their potential use as pharmaceutical agents. Of particular interest is the identification of 35 novel polypeptides that are potentially involved in immune response and inflammation mechanisms. A novel polypeptide has recently been identified that is expressed in mouse B cells in response to IL-4. The gene encoding this polypeptide is referred to as interfeukin-four induced gene 1, or "Fig.1" (Chu et al. Proc. Natl

Acad. Sci (1997) <u>94(6)</u>:2507-2512).

26. PRO1250

Long chain farry acid CoA ligace is an enzymatic protein that functions to ligate together long chain farry acids, a function that plays important roles in a variety of different physiological processes. Given the importance of this enzymatic protein, efforts are currently being undertaken to identify novel long chain fatty acid CoA ligace bottologs. We herein describe the identification and characterization of novel polypeptides having bomology to long chain fatty acid CoA ligase, designated herein as PRO1250 polypeptides.

PRO1475

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N-acrtylglucosaminyltransferase proteins comprise a family of enzymes that provide for a variety of important biological functions in the manumalian organism. As an example, UDP-N-acetylglucosamine: alpha-3-D-mannoside beat-1,2-N-acetylglucosaminyltransferase I is an enzymatic protein that caudyzes an essential first step in the conversion of high-mannose N-glycans to hybrid and complex N-glycans (Sarkar et al., <u>P10c. Nntl. Acad. Sci. USA</u>. 88:234-238 (1991). Given the obvious importance of the N-acetylglucosaminyltransferase enzymes, there is significant interest in the identification and characterization of novel polypopides having homology to an N-acetylglucosaminyltransferase protein. We herein describe the identification and characterization of novel polypopides having homology to an N-acetylglucosaminyltransferase protein, designated herein as PRO1475 polypopides.

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20 28. PRO1377

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypopride designated herein as PRO1377.

29. PRO13:

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Efforts are being undertaken by both industry and academia to identify new, native accreted proteins.

Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1325.

PRO1249

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Efforts are being undertaken by both industry and academia to Identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to 35 identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1249.

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II. PROIJIS

Many important cytokine proteins have been identified and characterized and shown to signal through specific cell surface receptor complexes. For example, the class II cytokine receptor family (CRF2) includes the interferon receptors, the interferont increments, the interferont increments of the class II cytokine receptor family (CRF2) includes the interferon receptors, the interferont increments of interferonts and the tissue factor CRFB4 (Spencer et al., <u>L.Exp.Med.</u> 187:571-578 (1998) and Kotenko et al., <u>EMBO J.</u> 16:5894-5903 (1997)). Thus, the multitude of biological activities exhibited by the various cytokine proteins is absolutely dependent upon the presence of cytokine receptor proteins on the surface of target cells. There is, therefore, a significant interest in identifying and characterization of a movel polypeptide having homology to cytokine receptor family-4 proteins, designated herein as PRO1315 polypeptides.

32. PRO1599

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Grazzyme M is a naural killer cell scrine protease. The human gene is 7.5 kilobases, has an exonintron structure identical to other scrine proteases, and is closely linked to the serine protease gene cluster on chromosome 19p13.3. (Pdist et al., Genomics, 24:445-450 (1994)). Grazzyme M has been found in two human 15 natural killer feukemia cell lines, unstimulated human peripheral blood monocytes and untreated purified CD3-CD56+ large granular lymphocytes. (Smyth et al., I. Immunol., 151:6195-6205 (1993)).

PRO1430

Reductases form a large class of enzymatic proteins found in a variety of mammalian tissues and play many important roles for the proper functioning of these tissues. They are antioxidant enzymes that catalyze the conversion of reactive oxygen species to water. Abnormal levels or functioning of reductases have been implicated in several diseases and disorders including strokes, heart stracks, oxidative stress, hypertension and the development of both benign and malignant tumors. For example, malignant prostate epithelium may have lowered expression of such antioxidant enzymes [Baker et al., <u>Prostate</u> 32(4):229-233 (1997)]. International patent application no. WO9622369-A1 describes a prostate specific reductase that is useful for diagnosing and treating prostate cancer and screening new antagonists. Inhibitors of alpha-reductase have been used in the treatment of benign prostatic hyperplasta (Anderson, <u>Drugs Asing</u> (1996) 6(5):388-396). For these reasons, the identification of new members of the reductase family has been of interest for the treatment and diagnosis of emercia and other diseases and disorders.

34. PRO13:

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Prolyl 4-byroxylase (P4HA) causlyzes the formation of 4-bydroxypeoline in collagens. Annunen, et al., I. Biol. Chem., 272(28):17342-17348 (1997); Helankosti, et al., PNAS USA, 92(10):4427-4431 (1995); and Hopkinson, et al., Gene, 149(2):391-392 (1994). This enzyme and molecules related thereto are of interest.

5. PROISI

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The terraspan family of proteins, also referred to as the "transmembrane 4 (TM4) superfamily", are

proposed to have an organizing function in the cell membrane. It is believed that they interact with large molecular complexes and function in such diverse activities as cell adhesion, activation and differentiation (see Mazecker et al. <u>FASEB</u> (1997) 11:428-442). Accordingly, the identification of new members of the tetraspan family of proteins is of interest. Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins.

36. PRO135

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Emerin is a cell surface protein associated with von Elner glands in mammals. Efforts are being undertaken by both industry and academia to identify new, native proteins and specifically those which possess sequence homology to cell surface proteins such as obserin or other salivary gland-associated proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins. We herein describe the identification of novel polypeptides having significant homology to the von Ebner minor salivary gland-associated protein, designated herein as PRO1357 polypeptides.

37. PRO124

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One type of transmembrane protein that has received attention is implantation-associated uterine protein. Deficiencies or abnormalities of this protein may be a cause of miscarriage. Therefore, the identification and characterization of implantation-associated proteins is of interest.

38. PRO1246

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Bone-related sulphanze is an ezzymatic protein that has been shown to degrade sulphaze groups of proteoglycan sugar chains in bone tissue (Australian Patent Publication No. AU 93/44921-A, March 3, 1994). Because of its specific sulphanase activity, it has been suggested that bone-related sulphanase may find use in the treatment of bone metabolic diseases. As such, there is significant interest in identifying and characterizing novel polypeptides having sequence similarity to bone-related sulphanase. We herein describe the identification and characterization of novel polypeptides having homology to bone-related sulphanase, designated berein as PRO1246 polypeptides.

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39. PRO135

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Clostridium perfringens emerotoxin (CPE) is considered to be the virulence factor responsible for causing the symptoms of C. perfringens type A food poisoning and may also be involved in other human and veterinary illnesses (McClane, Toxicon. 34:1335-1343 (1996)). CPE carries out its adverse cellular functions by binding to an approximately 50 kD cell surface receptor protein designated the Clostridium perfringens enterotoxin receptor (CPE-R) to form an approximately 90,000 kD complex on the surface of the cell., cDNAs encoding the CPE-R protein have been identified characterized in both human and mouse (Katahira et al., J. Cell Biol. 136:1239-1247 (1997) and Katahira et al., J. Biol. Chem. 272:26652-26658 (1997)). Since the CPE toxin

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has been reported to cause a variety of illnesses in mammalian hosts and those illnesses are initiated by binding of the CPE toxin to the CPE-R, there is significant interest in identifying novel CPE-R homologs. We herein describe the identification and characterization of novel polypeptides having homology to the CPE-R, designated herein as PRO1356 polypeptides...

40. PRO127

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the secrening of mammalian recombinant DNA libraries to identify the coding sequences for movel secreted proteins. We herein describe the identification and characterization of a novel secreted protein as PRO1275.

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Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1274.

PRO1412

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Efforts are being undertaken by both inclustry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammallan recombinant DNA libraries to demity the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1412.

43. PRO1557

The identification of secretory proteins that play roles in neural development are of interest. Such proteins may find use in the understanding of and possible treatment of neurological diseases and disorders. Chordin protein, which has been isolated from Xenopus, is a potent dorsalizing factor that regulates cell-cell interactions in the organizing centers of Xenopus head, trunk and tail development (Sasai et al., (1994) Cell 28(5):779-790; see also Mullins, (1998) Trends Genet, 14(4):127-129; and Kessel et al. (1998) Trends Genet, 14(5):109-171). It may be used as a component of culture medium for culturing nerve and muscle cells, and any have use in the treatment of neurodegenerative diseases and neural injury (U.S. Pat. No. 5,679,783).

4. PRO128

Efforts are being undertaken by both industry and scademia to identify new, native secreted proteins.

Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding
sequences for novel secreted proteins. We herein describe the identification and characterization of a novel
secreted protein designated herein as PRO1286.

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45. PRO1294

The extracellular mucous marrix of olfactory neurospithelium is a highly organized structure in intimate contact with chemosensory cilia that house the olfactory transduction machinery. The major protein component of this extracellular matrix is olfactomedin, a glycoprotein that is expressed in olfactory neurospithelium and which form intermolecular disulfide bonds so as to produce a polymer (Yokoe et al., Proc. Natl., Acad. Sci. USA 90:465-4659 (1993), Bal et al., Biochemistry 32:1047-1053 (1993) and Snyder et al., Biochemistry 39:143-9153 (1993)). It has been suggested that olfactomedin may influence the maintenance, growth or differentiation of chemosensory cilia on the spical dendritics of olfactory neurous. Given this important role, there is significant interest in identifying and characterizing novel polypeptides having homology to olfactomedin. We therein the identification and characterizing on or polypeptides having homology to olfactomedin protein.

10 We herein describe the identification and characterization of novel polypeptides having homology to offacumentin provein, designated herein as PRO1294 polypeptides.

PR0134

Buyrophilin is a milk glyopprotein that constitutes more than 40% of the total protein associated with the ontest of milk fat production toward the end pregnancy and is maintained throughout lactation. Butyrophilin has been identified in bovine, murithe and human (see Taylor et al., Blochin, Biophys, Acta 1306:1-4 (1996), Ishii et al., Blochin, Biophys, Acta 1245:285-292 (1995), Mather et al., L. Dairy Sci. 16:3832-3850 (1993), Ogg. et al., Manna, Genome, 7(12):900-905 (1996), Sato. et al., L. Biochem., 2011/1(1):147-157 (1995) and Banghart et al., L. Biol. Chem., 273:4171-4179 (1998)) and is a type I transmembrane protein that is incorporated into the fat globulin membrane. It has been suggested that butyrophilin may play a role as the principle scaffold for the assembly of a complex with xambine dehydrogenase/oxidase and other proteins that function in the budding and release of milk-fat globules from the apical surface during lactation (Banghart et al., Sugges). Given that butyrophilin plays a role in mammalian milk production, there is substantial statests in identifying novel butyrophilin homologs.

47. PRO1305

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins.

Many efforts are focused on the screening of mannantian recombinant DNA libraries to identify the coding 30 sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1305.

48. PRO1273

The lipocalin protein family is a large group of small extracellular proteins. The family demonstrates

35 great diversity at the sequence level; however, most lipocalins share characteristic conserved sequence motifs.

Lipocalins are known to be involved in retinol transport, invertebrate cryptic coloration, offaction and pheromone transport, and prostaglandin synthesis. The lipocalins have also been implicated in the regulation of cell

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homocostasts and the modulation of the immune response, and as carrier proteins, to act in the general clearance of endogenous and exogenous compounds. Flower, <u>Bischem, L</u>, 318(Pt 1):1-14 (1996); Flower, <u>FBBS Lett.</u> 354(1):7-11 (1994). Thus, novel members of the lipocalin protein family are of interest.

PRO1302

CD33 is a cell-surface protein that is a member of the sialoadhesin family of proteins that are capable of mediating sialic-acid dependent binding with distinct specificities for both the type of sialic acid and its linkage to subterminal sugars. CD33 is specifically expressed in early myeloid and some monocyte cell lineages and has been shown to be strongly associated with various myeloid numors including, for example, acute non-lymphocytic leukemia (ANLL). As such, CD33 has been suggested as a potential target for the treatment of cancers associated with high level expression of the protein. One CD33 homolog (designated CD33L) is described in Takei et al., Cytogenet. Cell Genet. 78:295-300 (1997). Another study describes the use of CD33 monocolonal analbodies in bone marrow transplantation for acute myeloid leukemia. Robertson, et al., Enga Clin. Biol. Rest., 389:47-63 (1994).

Moreover, studies have reported that members of the sialnadhesion family contribute to a range of macrophage functions, both under normal conditions as well as during inflammatory reactions. Crocker, et al., Giveoconi. 1., 14(5):601-609 (1997). Moreover, these proteins are associated with diverse biological processes, i.e., hemopoiesis, neuronal development and immunity. Kelm. et al., Giveoconi. 1., 13(6):913-926 (1996) Thus, novel polypeptides related to CD33 by sequence identity are of interest.

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SO. PKOIZE

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Olfacinry reception occurs via the interaction of odorants with the chemosensory citia of the olfactory receptor cells located in the nasal epithelium. Based upon the diversity of nasal epithelial-associated odorant binding proteins, the mammallan olfactory system is capable of recognizing and discriminating a large number of different odorant molecules. In this regard, numerous different odorant binding proteins and their encoding 25 DNA have recently been identified and characterized (Dear et al., <u>Biochemistry</u> 30: 10376-10382 (1991), Pevaner et al., <u>Science</u> 241:336-339 (1988), Buck et al., <u>Cell</u> 65:775-187 (1991) and Breer et al., <u>L. Recept. Res.</u>, 13:527-540 (1993)). Because study of the mechanisms of odorant detection by the mammalian olfactory system are of interest, there is significant interest in identifying movel odorant binding protein. We herein describe the identification and characterization of novel polypeptides having homology to odorant binding proteins, designated 30 herein as PRO1283 polypeptides.

. PRO1279

Protesses are enzymatic proteins which are involved in a large number of very important biological processes in mammalian and non-mammalian organisms. Numerous different protesse enzymes from a variety 35 of different mammalian and non-mammalian organisms have been both identified and characterized, including the serine protesses which exhibit specific activity toward various serine-containing proteins. The mammalian proteases enzymes play important roles in biological processes such as, for example, protein digestion, activation,

inactivation, or modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymen.

Neuropsin is a novel serine protease whose mRNA is expressed in the central nerrous system. Mouse neuropsin has been cloned, and studies have shown that it is involved in the hippocampal plasticity. Neuropsin has also been indicated as associated with extracellular matrix modifications and cell migrations. See, generally, Chen, et al., Neurosci., 7(2):5088-5097 (1995) and Chen, et al., <u>L. Histochem, Cytochem</u>, 46:313-320 (1998).

We berein describe the identification and characterization of novel polypoptides having homology to neuropsin protein, designated herein as PRO1279 polypoptides.

52. PRO130

- The immunophilits are a family of proteins that function as receptors for immunosuppressant drugs, such as cyclosporin A, FK506, and rapamycin. The immunophilina occur in two separate classes, (1) the FK506-binding proteins (FKBP3), which bind to FK506 and rapamycin, and (2) the cyclophilina, which bind to cyclosporin A. With regard to the FK506-binding proteins, it has been reported that the FK506/FKBP complex functions to inhibit the activity of the serine/threonine protein phosphatase 2B (calcineurin), thereby providing immunocsuppressant activity (Gold, Mol. Negrobiol. 15:285-306 (1997)). It has also been reported that the FK5BP immunophilins are found in the mammalian nervous system and may be involved in axonal regeneration in the central nervous system through a mechanism that is independent of the process by which immunosuppression is achieved (Gold, supra). Thus, there is substantial interest in identifying novel polypeptides having homology to the FK5BP immunophilins.
- 20 We herein describe the identification and characterization of novel polypeptides having homology to FK506 binding protein, designated herein as PRO1304 polypeptides.

53. PRO1317

- There is considerable interest in the identification of molecules whose expression is increased upon 25 stimulation of leukocyte populations because instights into the structure and function of these molecules may lead to further understanding of the intracellular and intercellular's events that accompany activation. One such molecule, CD97, a cell surface antigen that is rapidly upregulated upon activation on lymphocytes, has recently been the subject of several publications (see Eichler et al. in Tissue Amizena (1997) 20(2):479-438; Aust et al. Cancer Rea. (1997) 27(2):1798-1806). Leukocytes strongly positive for CD97 are concentrated at sites of inflammation relative to CD97 expression in normal lymphoid tissue. A soluble submit of CD97, CD97alpha, has been found in the body fluids from inflamed tissues (Gray et al. 1. Immunol. (1996) 127(12):5438-5447).
- 54. PRO1303
- Proteases are enzymatic proteins which are involved in a large number of very important biological

 35 processes in mammalian and non-mammalian organisms. Numerous different protease enzymes from a variety
 of different mammalian and non-mammalian organisms have been both identified and characterized, including
 the serine proteases which exhibit specific activity toward various serine-containing proteins. The mammalian

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process enzymes play important roles in biological processes such as, for example, protein digestion, activation, inactivation, or modulation of peptide bormone activity, and alteration of the physical properties of proteins and enzymes.

Neuropsin is a novel serine protease whose mRNA is expressed in the central nervous system. Mouse neuropsin has been cloned, and studies have shown that it is involved in the hippocampal plasticity. Neuropsin 5 has also been indicated as associated with extracellular matrix modifications and cell migrations. See, generally, Chen, et al., L.Neurosci., 7(2):5088-5097 (1995) and Chen, et al., L.Histochem, Cytochem, 46:313-320 (1998). Other studies have reported that kindling Induces neuropsin mRNA in the mouse brain. Okabe, et al., Brain Res., 728(1):116-120 (1996). Additionally, a study has reported that generation of reactive oxygen species has an important role in neuropsin transcript in the limbic areas which might be related to the disturbance in avoidance learning. Akita, et al., Brain Res., 769(1):86-96 (1997). Thus, neuropsins, and related proteins and agents, including agonists and antagonists are of interest.

PRO1306

There is much interest in the identification of proteins that play roles in mammalian disease and 15 disorders which could lead to new methods of treatment. A macrophage polypeptide, daimain/AIF1 inflammatory factor 1 (daimain/AIF1), has been identified in the pancreas of prodiabetic ruts, and has been determined to have a direct effect on insulia secretion. When injected intravenously in mice in low doses, dainain/AIF1 doses inhibited glucose-stimulated insulia secretion with a concominant impairment of glucose elimination. At higher doses, daintain/AIF1 potentiated glucose-stimulated insulia secretion with the pathogenesis of insulin-dependent diabetes mellitus (Chen et al. Pros., Natl. Acad. Sci., (1997) 94(25):13879-13889). AIF-1 has also been implicated in both rat and human allogenic beart transplant rejection (Utans et al. LClin., Invest., (1995) 95(6):2984-2962).

%. PRO1336

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Protein-protein interactions include receptor and strigen complexes and signaling mechanisms. As more is known about the structural and functional mechanisms underlying protein-protein interactions, protein-protein interactions can be more easily manipulated to regulate the particular result of the protein-protein interaction.

Thus, the underlying mechanisms of protein-protein interactions are of interest to the scientific and medical

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Leurine-rich proteins are known to be involved in protein-protein interactions. A study has been reported on leucine-rich proteoglycans which serve as itsue organizers, orienting and ordering collagen fibrills during ontogeny and are involved in pathological processes such as wound healing, tissue repair, and tumor stroma formation. Iozzo, R. V., Crit. Rev. Biochom. Mol. Biol., 32(2):141-174 (1997). Others studies implicating leucine rich proteins in wound healing and tissue repair are De La Salle, C., et al., Vouv. Rev. Ft. Hematol. (Germany), 37(4):215-222 (1995), reporting mutations in the leucine rich motifin a complex associated

with the bleeding disorder Bernard-Soulier syndrome and Chlemetson, K. J., <u>Thromb, Haemost</u>, (Germany) 74(1):111-116 (July 1995), reporting that platelets have leucine rich repeats.

Another protein of particular interest which has been reported to have leucine-rich repeats is the slit protein which has been reported to be useful in treating neuro-degenerative diseases such as Alzheinner's disease, neerve damage such as in Parkinson's disease, and for diagnosis of cancer, see, Artavanistsakonas, S. and Rothberg, J. M., WO9210518-A1 by Yale University. The slit protein has been characterized and reported to be secreted by glial cells and involved in the formation of axonal pathways in Drosophila as well as the mediation of extracellular protein interactions. Whereon and Crews, Mech. Dev., 40(3):141-154 91993); Rothberg and Artavanis-Tsakonas, L. Mol. Biol., 227(2):367-370 (1992); Rothberg, et al., Genes Dev., 4(12A):2169-2187 (1990); and Rothberg, et al., Cell. 55(6):1047-1059 (1988).

PRO127

Lywozymesare secreted enzymes that preferentially hydrolyze the [beta]-1,4 glucosidic linkages between N-acety/muranic acid and N-acety/gucowamine which occur in the mucopeptide cell wall structure of certain microoganisms. Lyeozyme is of widespread distribution in animals and plants. If has been found in mammalian secretions and tissues thetholing saliva, tears, milk, cervical mucus, leucocytes, kidacys, etc. The identification of new members of the hyzozyme family of proteins is of interest because of the variety of roles hyzozymes play in metabolic function and dysfunction. Abnormal levels of hyzozymes have been implicated in various disease states. Lysozymes have been reported to have anti-microbial, analgesic, and aninociceptive properties. Additional characteristics and possible uses of hyzozymes are described in U.S. Pat. No. 5,618,712.

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58. PRO129

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Glycosylation can determine the fate of a protein, for example, whether it is secreted or not. Also, glycosproteins play many structural and functional roles, particularly as part of the cell membrane. Therefore, glycosylation is of interest. Studies have reported on the growth-related coordinate regulation of the early N-glycosylation genes in yeast. Kukuruzinska and Lomon, <u>Glycobiology</u>, 4(4):437-443 (1994). Moreover, the relationship between protein glycosylation and farty acylation of glycosproteins was studied in the wild-type and separagine-linked glycosylation-deficient mutants in yeast. Appuluittan, <u>FEBS Lett.</u>, 255(1):139-142 (1989). The biosymbesis of asparagine-linked oligosarchanides in yeast was also studied using a mutant. Jackson, et al., <u>Glycobiology</u>, 3(4):357-364 (1993). Yeast mutants deficient in protein glycosylation have also been reported in Huffacher and Robbins, <u>PNAS</u>, 80(24):7466-7470 (1983).

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59. PRO1301

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Cytochrome P450 proteins form a large class of monooxygenase exzymes involved in hydroxylation. Hydroxylation reactions are important in the synthesis of cholesterol and steroid hormones. Enzymes of the 35 cytochrome P450 family play an important role in the metabolism endogenous compounds such as arachidonic acid. These enzymes are also important in the metabolism of foreign substances such as the elimination of drugs from the body [see, for example, Peterson, Aliment, Pharmacol, Ther., 9:1-9 (1995).]. In addition, metabolites

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generated through the cytochrome P450 pathway may play a role in carcinogenesis, blood pressure regulation and renal function [see, for example, Rahman et al., <u>Am. J. Hypertens.</u>, 10:356-365 (1997)].

60. PRO126

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO1268.

1. PKU120

Granulocytes, the most common type of white blood cell, have the ability to mediate immunologic cytoroxicity against tumor cells and microorganisms. Accordingly, there has been interest in identifying various factors that are produced by these cells because of their potential use as pharmaceutical agents. Patent publication no. W09729765-A1, to Selsted, describes the identification of granulocyte peptide A which was toolated from bovine and murine granulocytes. Several uses for this peptide were identified including, a 15 therapeutic use, use as an agricultural agent, use as a preservative for food, and use as a water treatment agent.

PRO132

Neurosophilin is a protein that was discovered as a neuronal glycoprotein that was coputified with neurosain I alpha during affinity chromatography on immobilized alpha-latrotoxin (Missier et al., L. Neurosoi. 18:3630-3638 (1998)). Recent data has shown that the mammalian brain contains four genes for neurexophilits the products of which share a common structure composed of five domains; (1) an N-terminal signal peptide, (2) a variable N-terminal domain, (3) a highly conserved central domain that is N-glycosylated, (4) a short linker region and (3) a conserved C-terminal domain that is cysteine-rich (Missier et al., supra). These data further demonstrate that the neurexophilitis are proceolytically processed after synthesis and bind to alpha-neurexins.

25 The structure and characteristics of neurexophilitis indicate that they may function as neuropeptides that may signal via alpha-neurexins. Therefore, there is significant interest in identifying and characterizing novel polypeptides having homology to the neurexophilins.

We herein describe the identification and characterization of novel polypeptides having bomology to accuracyhilin protein, designated herein as PRO1327 polypeptides.

63. PRO13

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Cerebellin is a secreted, posssynapte neuroprotein found throughout the brain. The highest concentrations of this protein have been found in the cerebellum. It has also been desected in the pinuitary, spinal cord, and afrenal glands (Satoh et al. L. Endocrinol., (1997) 15491):27-34). The feasibility of using cerebellum cord, and afrenal glands (Satoh et al. L. Endocrinol., (1997) 15491):27-34). The feasibility of using cerebellum and to chart a quantifiable marker for the investigation of the maturation of Purkinje cells of the cerebellum and to chart neurodevelopment has been reported (see Slemmon et al. Proc., Natl., Acad., Sci. (1985) 82/20):7145-7148). Significantly decreased levels of cerebellin have been found in human brains obtained in post-mortem studies.

from parients with spinocerebellar degeneration, olivopomocerebellar airophy (OPCAQ) and Shy-Drager syndrome, suggesting that cerebellin plays important pathophysiological roles in these cerebellar diseases (Mizumo et al. Brain Res. (1995) 666(1):115-118; Mizumo et al. No To Shinkei (1995) 47(11):1069-1074). In view of the importance of cerebellin in neurodevelopment and in neurological diseases and disorders, the identification and characterization of members of this protein family is of interest (see also Yiangou et al. Lengochem (1989) 53(2):186-889 and Mugnaini et al. Synance (1988) 27(1):125-138).

64. PRO1328

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to 10 identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide designated herein as PRO 1328.

65. PRO1325

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and
15 receptur proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to
identify the coding sequences for novel transmembrane proteins. We herein describe the identification and
characterization of a novel transmembrane polypeptide designated herein as PRO1325.

FRO1340

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Catherins are known as the principal mediators of homotypic cellular recognition and play a demonstrated role in the morphogenic direction of tissue development. Catherins are a diverse family of proteins that have been identified in various tissues including nervous tissue (Suzuki et al., Cell Regal, 2:261-270 (1991)). Kap-catherin is a kithery-specific member of the catherin multigene family (Thomson et al., Biol. Chem., 270:17594-17601 (1995)). Catherins are thought to play an important role in human cancer (Yap, Cancer Invest., 16:252-261 (1998)).

67. PRO1339

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a wide range of peptide hormones. Fricker, <u>Annu, Rev. Physiol.</u>, 50:309-321 (1988). This carboxypeptidase 30 has been associated with obesity. <u>Leiter, <u>L. Endocrinol.</u>, 155(2):211-214 (1997). Carboxypeptidase M has been reported as being a marker of macrophage maturation. Kraute, et al., <u>Immunol. Rev.</u>, 161:119-127 (1998). Human mast cell carboxypeptidase has been reported to be associated with allergies. Goldstein, et al., <u>Monost Alletex</u>, 27:132-145 (1990). Carboxypeptidase A2 has also been reported on. Faming, et al., <u>L. Biol. Chem.</u> 266(36):24606-24612 (1991). Other carboxypeptidases of particular macrest which are known in the art include 55 human pancreatic carboxypeptidase 2, carboxypeptidase al and carboxypeptidase B. Therefore, novel members of the carboxypeptidase family are of interest.</u>

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8. PRO1337

Of particular interest is the identification of blood-related proteins which may have potential therapeutic use or may be useful in the diagnosis of blood-related disorders. Thyroxine-binding globulin (TBG), is synthesized by the liver and secreted into the bloodstream. It is the principal thyroid hormone transport protein in human serum (Refenoff et al. Horm. Res. (1996) 45[3-5]; 128-138). High serum levels of TBG have been 5 found to cause hyperthyroxinaemia (Leahy et al., Postgrad Med. J. (1984) 60(703);324-327). Accordingly, the identification and characterization of TBG proteins is of interest (see Flink et al. Proc. Natl Acad Sci. USA (1986) 83(20);7708-7712; Darralena et al. Acad Med. Austriaca. (1988) 15 Suppl 1;17-15). Including the identification of abnormal TBG proteins (see Refetoff, Endoct Rev. (1989) [0/2);275-293). Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel 10 secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Pare. Natl. Acad. Sci., 92:7108-7113 (1996); U.S. Patent No. 5.536,637)].

PROLS

Efforts are being undertaken by both industry and academia to identify new, native transmembrane and
15 receptor proteins. Many efforts are focused on the serroning of mammalian recombinant DNA libraries to
identify the coding sequences for novel transmembrane proteins. We herein describe the identification and
characterization of a novel transmembrane polypeptide designated herein as PRO1142.

0. PRO1343

20 Efforts are being undertaken by both inclustry and academia to klentify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1243.

71. PRO1480

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in the nervous system. Members of the semaphorin family include both ligands and receptors. (Bethardt et al., Mol. Cell. Neurosci., 2: 409-419 (1997)). Studies have revealed a role for semaphorins in embryonic motor and central nervous system axon guidance and synapse formation. (Caralamo et al., Mol. Cell. Neurosci., 11: 30 173-182 (1998); Kitsukawa et al., Neuron, 12: 995-1005 (1997); Yu et al., Neuron, 20: 207-220 (1998)). Semaphorius have been shown to induce neuronal growth cone collapse and alter their pathway in vivo. (Shoji et al., Development, 125: 1275-1283 (1998)). Members of the semaphorin family have been shown to be immunologically active, inducing cytokine production in human monocytes. (Comean et al., Immunity, §: 473-482 (1998)). Semaphorius may also play a role in cancer. Expression of a mouse semaphorin gene is known 35 to correlate with metastatic ability in mouse numor cell lines. (Christensen et al., Cancer Res., 58: 1238-1244 (1998)).

- PRO1487

Fringe is a protein which specifically blocks serrate-mediated activation of notch in the dorsal compartment of the Drosophila wing imaginal disc (see Fleming et al., <u>Development</u>, 124(15):2973-81 (1997); Wu et al. Skience (1996) 273(5273):351-356). Fringe protein is also involved in vertebrate development where a thickening of the apital ecodermal edge essential for limb bud outgrowth involves an interaction between dorsal cells that express radical fringe and those that do not (see Wolpert, L. <u>Philos Trata R. Soc Lond B. Biol.</u> Sej. 1998) 333(1370):871-875; Kengaha et al. <u>Science</u> (1998) 280(5307):174-1277; Cohen et al. <u>Nature</u> (1997) 38(6523):360-372; Rodriguez-Exchen et al. <u>Nature</u> (1997) 38(6523):360-372; Rodriguez-Exchen et al. <u>Nature</u> (1997) 38(6523):360-372; Rodriguez-Exchen et al. Nature (1997) 38(6523):360-366).). Therefore, fringe protein is of interest for both is role in development as well as its ability to regulate serrate, particularly serrate's signaling abilities. Also of interest are novel polypeptides which may have a role in development and/or the regulation of serrate-like molecules. Of particular interest are novel polypeptides baving bornology to fringe-protein.

PRO1418

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins.
Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1418.

20 74. PRO1472

Buyrophilin is a milk glycoprotein that constitutes more than 40% of the total protein essociated with the fit globule membrane in mammalian milk. Expression of buyrophilin mRNA has been shown to correlate with the onset of milk fat production toward the end pregnancy and is maintained throughout lactation. Buyrophilin has been identified in bovine, murine and human (see Taylor et al., <u>Biochim, Biophys., Acta</u> 1306:1-4 (1996), Ishii et al., <u>Biochim, Biophys., Acta</u> 1245:285-292 (1995), Mather et al., <u>L. Dairy, Sei</u> 76:3832-3850 (1993), Ogg. et al., <u>Mamm., Genome.</u> 7(12):900-905 (1996), Sato, et al., <u>L. Biochem.</u> 117(1):147-157 (1995) and Banghart et al., <u>L. Biol. Chem.</u> 273:4171-4179 (1998)) and is a type I transmembrane protein that is incorporated into the fit globulin membrane. It has been suggested that buyrophilin may play a role as the principle scaffold for the assembly of a complex with xanthine dehydrogenase/oxidase and other proteins that function in the budding and release of milk-fat globules from the apical surface during lactanical interest in identifying novel buyrophilin homologs. Members of the buyrophilin family are further described in Tazi-Ahnini, et al., <u>Immunogenetics</u> 47(1):55-63 (1997); Davey, et al., <u>Gene.</u> 199(1-2):57-62 (1997); and Mather and Jack, <u>L. Dairy Sci.</u>, 76(12):3832-3850 (1993).

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75. PRO1461

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Proteases are enzymatic proteins which are involved in many biological processes in mammalian and

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non-mammalian organisms including digestion, protein activation and inactivation, modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes. Serine proteases comprise a large class of enzymes that exhibit specific activity toward various serine-containing proteins. Tryptin, which is synthesized by the pancreas and secreted to the small intestine, is a well-characterized serine protease that hydrolyzes peptide bonds of ingested proteins. Trypsin-like proteases have been characterized that are cell-surface proteins (see Farley et al. <u>Biochim Biophys Acta</u> (1993) <u>1173(3)</u>;350-357; and Leytus et al. <u>Biochemistry</u> (1988) <u>27(3)</u>;1057-1074). It is believed that some of these trypsin-like proteins may be synthesized as a membrane-bound procursor which matures to a soluble and active protease (Yamanaka et al. <u>L. Biol. Chem</u> (1998) 27(3):11895-11901).

Recause of there importance in metabolism and other enzymatic processes, efforts are being undertaket

10 by both industry and academia to identify new, native scrine-like proteases. Many efforts are focused on the
screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins.

6. PRO14

Efforts are being undertaken by both industry and aendemia to identify new, native transmembrane and

15 receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to
identify the coding sequences for novel transmembrane proteins. We herein describe the identification and
characterization of a novel transmembrane polypeptide designated herein as PRO1410.

PRO1568

The certaspanin (or tertaspan) family of proteins has grown to include approximately twenty known genes from various species. The tertaspanins are four transmembrane domain membrane-bound molecules which include for example, CD81, CD82, CD9, CD63, CD37 and CD53. Many of these proteins have a flair for promiscuous associations with other molecules, including lineage-specific proteins, integrins, and other transpanins. In terms of function, they are involved in diverse processes such as cell activation and proliferation.

25 adhesion and motility, differentiation and cancer. One study has proposed that these functions may all relate to their ability to act as "molecular facilitators", grouping specific cell-surface proteins and thus increasing the formation and stability of functional signaling complexes. Maecker, et al., FASEB, 11(6):428-42 (1997), Another study concludes that they are responsible for changes in cell morphology, cell-ECM adhesion and cell-algualing. Shabitz, et al., Limminglogy, 157:3617-3626 (1996). Thus, new members of this family are of 30 interest.

. PRO1570

Proteases are enzymatic proteins which are involved in many biological processes in mammalian and non-mammalian organisms including digestion, protein activation and inactivation, modulation of peptide 35 hormone activity, and alteration of the physical properties of proteins and enzymes. Serine proteases comprise a large class of enzymes that exhibit specific activity toward various serine-containing proteins. Trypsin, which is synthesized by the pancreas and secreted to the small intestine, is a well-characterized serine protease that

hydrolyzes peptide bonds of ingested proteins. Trypsin-like proteases have been characterized that are cellsurface proteins (see Farley et al. <u>Biochim Biophys Acta</u> (1993) <u>1173G1</u>);350-352; and Leyrus et al. <u>Biochemistry</u>
(1988) <u>27(3)</u>;1067-1074). It is believed that some of these trypsin-like proteins may be symbesized as a
membrane-bound precursor which matures to a soluble and active protease (Yamnoka et al. <u>L Biol. Chem</u> (1998)
273(19):11895-11901).

Of particular interest are human colon carcinoma derived serine proteases SP59, SP60 and SP67 which may be useful to screen for specific inhibitors or modulators to use in treatment of associated disease states and disorders related to these proteins. In Japanese patent J09149790-A, SP60 is reported to be identified, having accession number P_W22986 and 233 amino acids.

79. PROJ313

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Members of the semaphorin family of glycoproteins play important roles in the developing nervous system, and more particularly in exonal guidance. Semaphorins have been identified in the human immune system, where they are believed to play functional roles including B-cell signaling (Hall et al. Proc. Natl. Acad Sci (1996) 92/21);11780-50). A human semaphorin gene, useful in the diagnosis of nervous system an immune disorders, is disclosed in Japanese Pat. No. J10155490-A, published June 16, 1998. The identification of additional members of the semaphorin family if of interest.

. PRO178

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20 The enzymatic proteins that may be implicated in metabolic diseases or disorders are of paricular interest.

20 The enzymatic addition of sugars to fat-soluble chemicals is an important process that increases their solubility in water and aids in their excretion. In mammals, glucurould acid is the main sugar that is used to prevent the water products of metabolism and fat-soluble chemicals from reaching toxic levels in the body. The UDP glucuromosyltransferases that carry out this reaction are part of a super family of UDP glycosyltransferases found in animals, plants and bacteria. In the liver, UDP-glucuromosyltransferase conjugates bilirubin. There are a number of conditions which affect UDP-glucuromosyltransferase activity resulting in unconjugated byperbilirubinemia. These conditions include genetic disorders such as Crigler-Najjar Syndrome (see Jurgen et al., Blochem. J. (1996) 314:477-483) and Gilbert syndrome, as well as acquired conditions such as Lucey-Driscoll Syndrome. Accordingly, the idemification of novel members of the glucuromosyltransferase family is of interest (see Tukey et al., I. Biol. Chem. (1993) 268(20):15260-6; and WO9212287-A).

· CKOT490

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The cerebellum contains a bexadecapeptide, termed cerebellin, that is conserved in sequence from burnan to chicken. Three independent, overlapping cDNA clones have been isolated from a human cerebellum cDNA library that emcode the cerebellin sequence. The longest clone codes for a protein of 193 amino acids generally termed precerebellin, or a cerebellin precursor. This protein has a significant similarity to the globular region of the B chain of human complement component C1q. The region of relatedness extends approximately over 145 amino acids located in the carboxyl terminus of both proteins. Unlike C1q B chain, no collagen-like

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motifs are present in the animo-terminal regions of precerebellin. It is believed that cerebellin is not liberated from precerebellin by the classical dibasic amino acid proteabytic cleavage mechanism seen in many neuropeptide precursors. The cerebellin precursor has been associated with synaptic physiology. Urade, et al., PNAS_USA_88(3):1069-1073 (1991). Cerebellin, its precursor, and related molecules, particularly those having sequence identity with cerebellin, are therefore of interest.

. PRO143

Efforts are being undertaken by both industry and scademia to identify new, native transmembrane and receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We berein describe the identification and tharacterization of a novel transmembrane polypeptide designated herein as PRO1433.

PRO149

Enzymatic proteins play important roles in the chemical reactions involved in the digestion of foods the biosynthesis of macromolecules, the controlled release and utilization of chemical energy, and other processes 15 necessary to sustain life. Acyltransferases are enzymets which acylate moleties. For example, acyl-glycerol phosphate scyltransferases can act on lysophosphatidic acid as a substrate. The lysophosphatidic acid is converted to phosphatidic acid and thus plays a role in forming phosphatidylethanolamine found in membranes. Sec., Brown, et al., Plant Mol. Biol., 26(1):211-223 (1994). Moreover, 1-acyl-sn-glycerol-3-phosphate acyltransferase (LPAAT) is an enzymatic protein that shows a preference for medium-chain-length fatry acyl 20 concuyrne A substrates. Sec, Kautson et al., Plant Physiol., 109:999-1006 (1995)). Thus, acyltransferases play an important role in the biosynthesis of molecules requiring acylation.

We berein describe the identification and characterization of novel polypeptides having homology to a leasyl-an-glycerol-3-phosphate acyltransferase protein, designated herein as PRO1490 polypeptides.

25 84. PRO1482

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the secretning of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO 1482.

85. PRO144

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Efforts are being undertaken by both industry and academia to identify new, native secreted proteins.

Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1446.

. KKUISS

Methyltransferase enzymes enalyze the transfer of methyl groups from a donor molecule to an acceptor molecule. Methyltransferase enzymes play extremely important roles in a number of different biological processes including, for example, in the electron transport chain in the plasma membrane in prokaryotes and in the inner mitochondrial membrane in cukaryotic cells (see, e.g., Barkovich et al., <u>L. Bjol. Chem.</u> 272:9182-9188 (1997), Dibrov et al., <u>L. Bjol. Chem.</u> 272:9175-9181 (1997), Lee et al., <u>L. Bacteriol.</u> 179:1748-1754 (1997) and Marbois et al., <u>Arch. Bjochem.</u> 2jochem. 2j

87. PRO1604

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The identification of novel growth factors is of particular interest because of the roles they play in inducing cellular growth, proliferation and differentiation in both normal states and abnormal states. The identification of growth factors that are over- or under-expressed in abnormal tissues (e.g. numors) may lead to the development of diagnostic tools and therapeutic agents. Growth factors have been isolated from hepatoma-derived cell lines. Hepatoma-derived growth factors have been isolated from mouse (Japanese Pat. No. 109313185-A, published December 9, 1997) and human (Japanese Pat. No. 106343470-A, published December 9, 1997) and human (Japanese Pat. No. 106343470-A, published December 9, 1997) and human (Japanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published December 9, 1997) and human fapanese Pat. No. 106343470-A, published from human fapanese Pat. No. 106343470-A, published from human fapanese Pat. No. 106343470-A, published from

25 88. PRO1491

The neuronal cell body is usually round like any other cell. However, these cells have structures, also referred to as "processes", which grow from them to form synaptic connections. Some of these processes earry information away from the cell body; sometimes over very long distances. These long and thin processes are axons. The axon is a thin, static tube. Other processes carry information either towards the cell body, or both towards and away from the cell body. These shorter and usually thicker processes are called dendrites. Both axons and dendrites are called neurics.

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During development and the growth stage of neurous, neurites are formed by means of growth cones. A growth cone is the growing tip of a neurite. The growth cone is flattened and bighly motile. It is where new material is added and further extension of the axon originates. Controlling where the growth cone crawls controls were the axon will be laid down and thus where it will be present.

The growth cone has several definable parts. The thin, flattened, vell-like processes that stick out and retract from the leading edge are called lamellipodia. The needle-like processes that stick out and retract from

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the leading edge are called microspikes or filopodia. These are the structures involved in pushing the leading edge of the growth come forward.

The accurate navigation of growth cones to their appropriate targets requires that they recognize any respond to navigational cues in their immediate environmem. Some of these cues encourage extension into others. Well characterized molecules that encourage neurite outgrowth in vitro include the extracellular matrix molecule laminin and the neuronal cell surface molecule L1/G4/8D9. These molecules which promote neurite extension are generally widely distributed throughout the body. Laminin immunoreactivity is reasonably widespread in the developing central and perlyheral nervous systems. Similarly, L1/G4/8D9 is present on a wide variety of neuronal processes in the developing central nervous system, particularly long projecting axons. It is, therefore, unclear whether the known outgrowth promoting molecules play an important role in self-specific choices growth cones make as they decide between possible routes. Instead, their function is believed to provide a generally permissive environment in which growth cones extend and respond to more specific navigational cues.

Among these more specific cues are molecules that inhibit the motility of particular growth cones. Growth cones have been observed to lose their motile morphology and cease advancing (collapse) on contact with other neurites of different types. Territory formation in vitro may mean the manifestation of a process that leads to selective fasciculation in vivo. Some growth comes have been observed to crawl along specific axonal pathways, or sterrootype sequences of axonal pathways in developing embryos. Specific motility inhibiting effects could determine which of several alternative pathways a growth cone will extend on. Growth cones would be expected to prefer growing on axons that do not induce them to collapse while shumning those that do.

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It has been observed that, for example, sympathetic growth cones will be inhibited or collapse when coming in contact with retinal neurites. Likewise, growth cones of retinal neurites will collapse when coming in contact with sympathetic neurites. It is believed that such cell activity is achieved through the presence of receptors which specifically respond to specific growth inhibition coses by the molecules which transmit specific cues pertaining to growth. Cues are believed to be present on cell surfaces, particularly on axon surfaces.

When nerve damage occurs, repair is impeded or incapable of occurring due to the fallure of neurites to replace damaged axons or dendrites. If an existing neurite is damaged, severed or destroyed, a new neurite is incapable of growing out from the cell body to replace it. The presence of molecules which thibbit neurite growth are believed to be responsible for the difficulty in neurite regeneration. Collapsins are proteins that function to modulate the activity of molecules which modulate growth come extension.

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We herein describe the identification and characterization of novel polypeptides having homology to a collapsin protein, designated herein as PRO1491 polypeptides.

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89. PRO1431

The transduction of intracellular signaling is crucial to cell processing such as differentiation, motility

35 and division. Such signal transduction is believed to occur throughout the cell in the form of complex interactions between proteins. Such protein-protein interactions are often mediated by modular domains within signaling proteins. As a result, signal transduction is now modeled as a system in which molecules act in a

combination, and the composition of that combination, determines the signal

Sre bomology domains (e.g., SH2 and SH3) are two domains found in regions of sequence similarity of proceins involved in signal transduction. Early work on the oncogenite tyrosine kinese Sre identified the SH2 domain. Since then, SH2 and SH3 domains have been found in many diverse proceins, making them among the most common type of structural motif. SH2 and SH3 domains are modular in that they fold independently of the protein that contains them, their secondary structure places N- and C- terminal close to one another in space, and they appear at variable locations (anywhere from N- to C-terminal) from one protein of the next (Cohen et al., Cell 80: 237-348, 1995).

Early studies that mutated the SH2 or SH3 domain showed that these two domains were important for function, but it was not until the cloning of unrelated families of signaling proteins such as RAS-GAP, and the Crk oncogene that the modular nature of these domains was revealed. These latter experiments demonstrated that RAS-GAP and Crk bound tightly to receptor tyrosine kinases upon ligand stimulation. Follow-up studies demonstrated that the mechanism of this binding was through the SH2 domain and that receptor autophosphorytation was required. Such a finding implied that activation of the receptor tyrosine kinase could be viewed as a means of changing the binding aspect of the intracellular domain, and the receptor-SH2 containing protein interaction would initiate the signal transduction cascade.

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SH3 domains have a more general function than that which is purported for SH2. SH3 binding proteins have been isolated by screening buckeriophage expression libraries with labeled SH3 domains. The results of these experiments showed that SH3 domains would bind to short proline-rich peptides, in particular the motif PxxP. Based on the level of knowledge present at the time of the preparation of the present patent application, all of the SH3 binding sites identified have the property of being proline rich. Binding of an SH3 domain is independent of covalent modification of the binding site, such as phosphorylation as occurs with the SH2 domain. As a result, SH3-ligand interactions are usually constitutive and not inducible, although exceptions do exist. In general, SH3 domains are less likely to act as signal /twitners* than as a means of assembling protein complexes via moderate-affinity interactions. Such moderate affinity interactions also imply that the SH3-mediated interactions will be relatively short in duration and remodeled in response to changes in concentration of binding

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The resolution of binding characteristics of SH2 and SH3 domains has led to proposed compounds which would block signal transduction. Peptidomimetic ligands based on the sequence of target proteins for SH2 and SH3 domains may represent new lead compounds for the therapy of proliferative diseases that are dependent upon constitutively activated tyrosine kinases (e.g., BCR/ABL in chronic myelogenous and acute lymphocytic leukemias or HER-2/Neu in breast and ovarian cancer).

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90. PRO156

Cellular disintegrin and metalloproteinase (ADAMs) are a family of genes with a sequence similar to 35 those of snake venom metalloproteinases and disintegrins. The ADAMTS-1 gene encodes a new type of ADAM protein with respect to possessing the thrombospondin (TSP) type I motifs, the expression of which is associated with the inflammatory process (Kuno et al., <u>L. Biell. Chem.</u>, 273:13912-13917 (1998), Kuno et al., <u>Genomics</u>

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46:466-471 (1997) and Kuno et al., <u>J. Biol. Chem.</u> 272:556-562 (1997)). Expression of the ADAMTS-I gene is induced in kidney and heart by *in vivo* administration of lipopolysaccharide, suggesting a possible role in the inflammation reaction. In this regard, the ADAMTS-I protein has been suggested as phying a possible role in various inflammatory processes as well as in the development of camere cachestia (Kuno et al., 1998, supra). We berein describe the identification and characterization of novel polypeptides having homology to ADAMTS-I protein, designated herein as PRO1563 polypeptides.

PKOIS

Chondromodulin proteins are earthago-generated matrix components that synergistically stimulate the growth and differentiation of chondrocytes (Suznki, Connect, Tissue Res. 35:303-307 (1996)). More specifically, chondromodulin-I functions to inhibit the proliferation of vascular endothetial cells and tube formation, thereby functioning to stimulate cartilage growth and inhibiting replacing cartilage by bone in an early stage. Chondromodulin-II, while not capable of inhibiting vascularization like chondromodulin-I, also functions to stimulate osteoclass differentiation and cartilage growth. As such, these two polypeptides are essential for the regulation of the formation of cartilage and endochondral bone structures. Given the extremely important 15 physiological roles played by the chondromodulin proteins, there is significant interest in identification and characterization of novel polypeptides having bomology to these proteins. We herein describe the identification and characterization of novel polypeptides having homology to chondromodulin-I protein, designated herein as PRO1565 polypeptides.

92. PRO1571

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Clearidium perfringens enterwoxin (CPE) is considered to be the virulence factor responsible for causing the symptoms of C. perfringens type A food poisoning and may also be involved in other human and veterinary illnesses (McClane, Toxicon: 34:1335-1343 (1996)). CPE carries out its adverse cellular functions by binding to an approximately 50 kD cell surface receptor protein designated the Clostridium perfringens catterwoxin receptor (CPE-R) to form an approximately 90,000 kD complex on the surface of the cell. cDNAs encoding the CPE-R protein have been identified characterized in both human and mouse (Katabira et al., J. Biol. Chem. 272:26652-26658 (1997)). Since the CPE toxin has been reported to cause a variety of Illnesses in mammalian bosts and those illnesses are initiated by binding of the CPE toxin to the CPE-R, there is significant interest in identifying novel CPE-R homologs. We harrein describe the identification and characterization of novel polypeptides having homology to the CPE-R, designated barein as PRO1679 polypeptides.

3. PRO1572

Clostridium perfringens enterotoxin utilizes two structurally related membrane proteins as functional

receptors in vivo. Human and mouse cDNAs showing bomology to the Clostridium enterotoxin receptor (CPBR) gene have previously been cloned as described in Katahira, et al., L. Biol. Chem. 272(42):26652-8 (1997).

They have been classified into two groups, the Vero cell CPE receptor homologues and rat androgen withdrawal

apoptosis protein (RVPI). These receptors are thus of interest as are related molecules. Of particular interest is the use of these receptors and related molecules in the identification of modulators of these receptors.

Also of interest are members of the claudin family and molecules related thereto. Claudins are integral membrane proteins localizing at tight junctions with no sequence similarity to occludin. Furuse, et al., <u>I.Cell Biol.</u>, 141(7):1539-50 (1998).

. PRO1573

Clostrichm perfringens enterocoxin utilizes two structurally related membrane proteins as functional receptors in vivo. Human and mouse cDNAs showing homology to the Clostrichum enterotoxin receptor (CPE-R) gene have previously been cloned as described in Katahira, et al., <u>J. Biol. Chem.</u>, 272(42):26652-8 (1997). They have been classified into two groups, the Vero cell CPE receptor homologues and rat androgen withdrawal apoptosis protein (RVP1). These receptors are thus of interest as are related molecules. Of particular interest is the use of these receptors and related molecules in the identification of modulators of these receptors.

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Also of interest is the ventral proxate. I protein (RVP-I) which is transcriptionally induced in the regressing rat prostate after castration. This protein is further described in Peacock, et al., <u>Genomics</u>, 46(3):443-9 (1997).

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Clostridium perfringens enterotoxin utilizes two structurally related membrane proteins as functional receptors in vivo. Human and mouse cDNAs showing homology to the Clostridium enterotoxin receptor 20 (CPE-R) gene have previously been closted as described in Katahira, et al., <u>L. Biol. Chem.</u>, 272(42):26652-8 (1997), and Katahira, et al., <u>1. Cgll Biol.</u>, 136(6):1239-1247 (1997). They have been classified into two groups, the Vero cell CPE receptor homologues and rat androgen withdrawal apoptosis protein (RVP1). These receptors are thus of interest as are related molecules. Of particular interest is the use of these receptors and related molecules in the identification of modulators of these receptors.

25 Efforts are being undertaken by both industry and academia to identify new, native receptor proteins.
Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins.

PROLES

Occaridium perfringens entertotain (CPE) is considered to be the viralence factor responsible for causing the symptoms of C. perfringens type A food poisoning and may also be involved in other human and venerthary illnesses (McClane, Toxicon. 34:1335-1343 (1996)). CPE carries out its adverse cellular functions by binding to an approximately 50 kD cell surface receptor protein designated the Clostridium perfringens entertoxin receptor (CPE-R) to form an approximately 90,000 kD complex on the surface of the cell. cDNAs exceeding the CPE-R protein have been identified characterized in both human and mouse (Katahira et al., J. Biol. Chem. 272:26652-26658 (1997)). Since the CPE toxim has been reported to cause a variety of illnesses in mammalian hosts and those illnesses are initiated by binding

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of the CPE toxin to the CPE-R, there is significant interest in identifying novel CPE-R homologs. We herrin describe the identification and characterization of novel polypeptides having homology to the CPE-R, designated herein as PRO1489 polypeptides.

97. PRO14

Avian egg whites are a rich source of protein inhibitors of proteinases belonging to all four mechanistic classes. Owomocoid and ovoinhibitor are multidomain Kazal-type inhibitors with each domain containing an actual or putative reactive site for a seriae proteinase. Cystatin is a cysteine proteinase inhibitor, white ovostatin inhibits proteinases of all four mechanistic classes. For a review of these inhibitors, see Saxena and Tayyab, Cell Mol. Life Sci., 53(1):13-23 (1997). New members of protein inhibitors of proteinases are of interest, 10 particularly those having sequence identity with known inhibitors such as ovonucoid.

Serine protease inhibitors in general are of interest. Serine proteases such as neuropsin have been indicated as associated with extracellular matrix modifications and cell migrations. See, generally, Chen, et al., Neurossi, 7(2):5088-5097 (1995) and Chen, et al., L. Histochem, Cotochem, 46:313-320 (1998). Another sterine protease, the enamel matrix serine proteinase, is associated with the degradation of organic matrix in teeth. Simmer, et al., L. Dent. Res., 77(2):377-386 (1998), Overall and Limeback, Biochem L. 256(3):965-972 (1988), and Moradian-Oldak, Comnect, Tistue Res., 35(1-4):231-238 (1996). Thus, inhibitors of these proteases are of interest in the case that these mechanisms require control.

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PRO1508

20 Efforts are being undertaken by both industry and academia to identify new, native secreted proteins.
Many efforts are focused on the acreening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1508.

99. PRO1555

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Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designance herein as PRO1555.

00. PRO1485

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Lyzozymes are secreted enzymes that preferentially bydrolyzethe [beta]-1,4 glucosidic linkeges between N-acctylmuramic acid and N-acctylgucotamine which occur in the mucopeptide cell wall structure of certain microogenisms. Lysozyme is of widespread distribution in animals and plants. It has been found in mammalian secretions and tissues including saliva, tears, milk, cervical mucus, leucocytes, kitheys, etc. The identification of new members of the lysozyme family of proteins is of interest because of the variety of roles lysozymes play in metabolic function and dysfunction. Abnormal levels of hysozymes have been implicated in various disease

states. Lysotymes have been reported to have anti-microbial, analgesic, and aninociceptive properties. Additional characteristics and possible uses of hysotymes are described in U.S. Pat. No. 5,618,712.

Of particular interest is lysozyme C which has been recrulted as a digestive enzyme in the stomachs of creatures needing to retrieve nutrients from microorganisms in fermented frod. The history of lysozyme C and related proteins are further described in Qasba and Kumar, <u>Crit. Rev. Biochem. Mol. Biol.</u>, 32(4):235-306 (1997); Irwin. <u>EXS</u>, 75:347-361 (1996)

101. PRO156

Glycoxylation is a common and complex form of post-translational protein modification. Although a large and increasing number of unique structures is known to exist, most arise from a series of common synthetic intermediates and differ at their periphery glycosylutansferases, which recognize both the oligosaccharide acceptor and features of the underlying protein. UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase is an enzymatic protein that initiates O-glycosylation of specific serine and threonine antino acids in proteins by adding N-acetylgalactosamine to the hydroxy group of these amino acids. Since numerous important biological and physiological evenus are regulted by protein glycosylation, there is significant interest in identifying and characterizing novel polypeptides having homology to the known glycosylation proteins. We herein describe the identification and characterization of novel polypeptides having homology to an N-acetylgalactosaminyltransferase protein, designated herein as PRO1564 polypeptides.

102. PRO175

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Efforts are being undertaken by both industry and academia to identify new, native transmembrane proceins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1755.

25 103. PROJ<u>757</u>

Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the eccenning of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1757.

104. PRO1758

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Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein as PRO1758.

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105 PRO1575

Protein Distiffed Isomerase (PDI) enhances formation of distiffed bonds in human strum albumin (HSA). Consequently, PDI assists in the formation of the overall structure of human strum albumin. Co-corpression of PDI with human strum albumin increases secretion of HSA by reducing the chance of HSA structural instability and destruction by cellular proteases. Co-expression of PDI and HSA improved localization in the endoplasmic treix-ulum of eukaryotic cells. (Hayano et al., EP-50941-A (1992)). PDI and the beta-enbunit of human prolyl 4-hydroxylase have been shown to be products of the same gene. (Phhajaniemi et al., EMBC L. 6:643-49 (1987)). In addition, copies of the CGHC-containing active site sequences of PDI have been found in an abundant luminal endoplasmic reticulum protein, Erp72. (Mazzarella et al., 1, 1, 1, 100, Chem., 2:1094-1101)

10 Efforts are being undertaken by both industry and academia to identify new, native receptor proteins.
Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins.

106. PRO1787

Multiple de novo MPZ (PO) point mutations have been identified in a sporadic Dejerine-Sottas (DDS) case. Warner, et al., Hum. Mutat., 10(1):21-4 (1997). DDS is a sovere demyelinating peripheral neuropathy with onset in infancy, and has been associated with mutations in either PMPZ2 or MPZ. Morsover, mutational analysis of the MPZ, PMP22 and Cx32 genes in patients of Spanish ancestry with Charcot-Marie-Tooth disease and hereditary neuropathy with liability to pressure patsies have been reported on. Bort, et al., Hum. Genet., 20 99(6):746-54 (1997). Myelin glycoprotein PO has been reported on in a number of other studies as well (Blanquet-Grossard, et al., Clin. Genet., 48(6):281-3 (1995), Haytsuka, et al., Nat. Genet., 5(1):31-4 (1993) and Saavedra, et al., J. Mol. Evol., 29(2):149-56 (1989). Thus, proteins which may belong to the myelin pd family are of interest.

25 107. PRO1781

Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammallan recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1781.

108. PRO15

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Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1556.

. PRO175

Efforts are being undertaken by both inclustry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1759.

110. PRO176

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein as PRO1760.

111. PR01561

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Phospholipase A2 (PLA2) is a protein which hydrulyzes a 2-acyl ester bond of phospholipids, and examples thereof include cytosotic PLA2 and eccretory PLA2 which can be clearly distinguished from each other. It has been known that the cytosotic PLA2 (cPLA2) selectively hydrolyzes phospholipids containing arachidomic acid of which 2-position is esterified. Given these important biological activities, there is significant interest in identifying and characterizing novel physpeptides having homology to phospholipase A2 proteins. We herein describe the identification and characterization of novel polypeptides having homology to human phospholipase A2 protein, designated herein as PRO1561 polypeptides.

112. PRO156

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Colon specific genes (CSGs) and their expression products are described in published international application WO9639419. They are useful diagnostic markers for colon cancer and for colon cancer metastasis and can also be used to screen for potential pharmaceutical and diagnostic agents. The identification of new members of the CSG family is of interest.

113. PRO1693

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Insulin-like growth factors have both growth spronoting and insulin-like activities. There are two well characterized plasma IGF-binding proteins in human. The larger protein is an acid-labile protein of 53K which itself and an acid-labile protein of 55K which itself and an acid-labile non-IGF-binding protein with an approximate molecular mass of 100K kD. The smaller protein has an apparent molecular mass of 28K in the non-reduced form and 34K when reduced. These IGF-binding proteins have been shown to play important roles in the physiological activities played by the insulin-like growth factor proteins. As such, there is substantial interest in identifying and characterizing novel polypeptides having homology to the Insulin-like growth factor binding proteins. We herein describe the identification and characterization of novel polypeptides having homology to an insulin-like growth factor binding protein, designated herein as PRO1693 polypeptides.

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114. PRO178

Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane protein designated herein as PRO1784.

PRO16

N-acetylglucusaminyltransferase proteins comprise a family of enzymes that provide for a variety of important biological functions in the mammalian organism. As an example, UDP-N-acetylglucusamine: alpha-3D-mannoside bear-1,2-N-acetylglucusaminyltransferase I is an enzymatic protein that catalyzes an essential first
step in the conversion of high-mannose N-glycans to hybrid and complex N-glycans (Sarkar et al., Proc. Natl
Acad. Sci. USA, 88:234-238 (1991). Given the obvious importance of the N-acetylglucusaminyltransferase
enzymes, there is significant interest in the identification and characterization of novel polypeptides having
homology to an N-acetylglucusaminyltransferase protein. We herein describe the identification and
characterization of novel polypeptides having homology to an N-acetylglucusaminyltransferase protein.

116. PRO1788

Protein-protein interactions include receptor and antigen complexes and signaling mechanisms. As more is known about the structural and functional mechanisms underlying protein-protein interactions, protein-protein 20 interactions can be more easily manipulated to regulate the particular result of the protein-protein interaction.

Thus, the underlying mechanisms of protein-protein interactions are of interest to the scientific and medical community.

Profeins containing leucine-rich repeats are thought to be involved in protein-protein interactions.

Leucine-rich repeats are short sequence motifs present in a number of proteins with diverse functions and cellular

25 locations. The crystal structure of ribonuclease inhibitor protein has revealed that leucine-rich repeats

correspond to beta-alpha structural units. These units are arranged so that they form a parallel beta-sheet with

one surface exposed to solvent, so that the protein acquires an unusual, nonglobular shape. These two features

have been indicated as responsible for the protein-binding functions of proteins containing leucine-rich repeats.

Sec, Kobe and Deisenhofer, Trends Biochem. Sci., 19(10):415-421 (Oct. 1994).

A study has been reported on leucine-rich proteoglycans which serve as tissue organizers, orienting and ordering collagen fibrils during omogeny and are involved in pathological processes such as wound healing, itssue repair, and numor stroma formation. Iozzo, R. V., <u>Crit. Rev. Blochem. Mol. Biol.</u>, 22(2):141-174 (1997). Others studies implicating leucine rich proteins in wound healing and tissue repair have been reported including De La Salle, C., et al., <u>Vouv. Rev. Fr. Hematol.</u> (Germany), 37(4):215-222 (1995), reporting mutations in the leucine rich modif in a complex associated with the bleeding disorder Bernard-Soulier syndrome: Chlemetton, K. J., <u>Thromb. Haemost</u>. (Germany), 74(1):111-116 (July 1995), reporting that platelets have leucine rich repeats and Ruostlahi, E. I., et al.; and WO9110727-A by La Iolla Cancer Research Foundation,

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reporting that decorin binding to transforming growth factor-at has involvement in a treatment for cancer, wound healing and scarring. Related by function to this group of proteins is the insulin like growth factor (IGF), in that it is useful in wound-healing and associated therapies concerned with re-growth of tissue, such as connective tissue, with and hone; in promoting body growth in humans and animals; and in stimulating other growth-related processes. The acid labile subunit of IGF (ALS) is also of interest in that it increases the half-life of IGF and is part of the IGF complex in vivo. Ollendorff, V., et al., Cell Growth Differ, 5(2):213-219 (Pcb. 1994; identified the GARP gene which encodes a leucine-rich repeat-containing protein that has structural similarities with human GP its alpha and GP V platelet proteins, and with the Chaoptin, Toll, and Connectin adhesion molecules of Drosophila.

Another protein which has been reported to have leucine-rich repeats is the SLTI protein which has been lin Parkinson's disease, and for diagnosts of cancer, see, Artavanitsakonas, S. and Rothberg, J. M., WO9210518-A1 by Yale University. Of particular interest is LIG-1, a membrane glycoprotein that is expressed specifically in glial cells in the mouse brain, and has leucine rich repeats and immunoglobulin-like domains. Suruki, et al., <u>L. Biol., Chem.</u> (U.S.), 271(37):22522 (1996). Other studies reporting on the biological functions of proteins having leucine rich repeats inchale: Tayar, N., et al., <u>Mol., Cell. Endocrinol.</u>, (Ireland) 125(1-2):65-70 (Dec. 1996) (gonadorropin receptor involvement); Miura, Y., et al., <u>Mippon Ritasto</u> (Japan) 54(7):1784-1789 (July 1996) (gonadorropin receptor involvement); Arris, P. C., et al., <u>L. Am., Soc., Nephrol.</u> 6(4):1125-1133 (Oct. 1995) (didney disease involvement); and Almeida, A., et al., <u>Oncogene</u> 16(22):2997-3002 (June 1998) (malignant glioma involvement).

117. PRO180

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Interleukin-10 (IL-10) is a pleiotropic immunosuppressive cytokine that has been implicated as an important regulator of the functions of myeloid and lymphoid cells. It has been demonstrated that IL-10 functions as a potent inhibitor of the activation of the synthesis of various inflammatory cytokines including, for example, IL-1, IL-6, IFN-y and TNF-a (Gesser et al., <u>Proc. Natl. Acad. Sci., USA</u> 94:14630-14625 (1997)). Moreover, IL-10 has been demonstrated to strongly inhibit several of the accessory activities of macrophages, thereby functioning as a potent suppressor of the effector functions of macrophages, T-cells md NK cells (Kuhn et al., <u>Cell</u> 75:263-274 (1993)). Furthermore, IL-10 has been strongly implicated in the regulation of B-cell, mass cell and thymocyte differentiation.

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30 II.-10 was independently identified in two separate lines of experiments. First, cDNA clones encoding murine II.-10 were identified based upon the expression of cytokine synthesis inhibitory factor (Moore et al., Science 248:1230-1234 (1990)), wherein the human II.-10 counterpart cDNAs were subsequently identified by cross-hybridization with the murine II.-10 cDNA (Viera et al., Proc. Natl. Acad. Sci. USA 88:1172-1176 (1991)). Additionally, II.-10 was independently identified as a B-cell-derived mediator which functioned to co-

Recently, a novel cytokine polypeptide which is member of the IL-10-related cytokine family has been identified and characterized. This novel secreted cytokine, designated IL-19, is a 177 amino acid polypeptide

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having a molecular weight of approximately 20.4 LD (see WO 98/08870, published March 5, 1998). It has been reported that IL-19 is specifically expressed by activated monocytes, wherein increased and/or decreased levels of IL-19 may be associated with one or more physiological disorders that are associated with increased or decreased levels of cytokine production (see WO 98/08870). Specifically, IL-19 is suggested as being capable of inhibiting the symbesis of inflammatory cytokines by cells of the immune system.

Given the obvious importance of the various cytokine polypeptides and, more specifically, immunosuppressive cytokines such as IL-10 and potentially IL-19, there is significant interest in the Identification and characterization of novel cytokine polypeptides having homology to IL-10 and/or IL-19. We herein describe the identification and characterization of novel polypeptides having homology to IL-19, designated herein as PRO1801 polypeptides.

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118. UCP4

Uncoupling proteins or "UCPs", believed to play a role in the metabolic process, have been reported in the literature. UCPs were first found and described in the brown fat cells of bibernating animals, such as bears. UCPs were believed to help such hibernators and other cold-weather adapted animals maintain core body for the properties of cold weather by raising their body's resting metabolic rate. Because humans possess relatively small quantities of brown adipose tissue, UCPs were originally thought to play a minor role in human metabolism.

Several different human uncoupling proteins have now been described. [See, generally, Gura, Science 280:1369-1370 (1998)]. The human uncoupling protein referred to as UCP1 was identified by Nicholls et al. 20 Nicholls et al. showed that the inner membrane of brown fat cell mitochondria was very permeable to proteins and the investigators traced the observed permeability to a protein, called UCP1, in the mitochondrial membrane. Nicholls et al. reported that the UCP1, by creating such permeability, reduced the number of ATP3 that can be made from a food source, thus raising body metabolic rate and generating heat. [Nicholls et al., Physiol. Rev., 64, 1-64 (1994)].

25 It was later found that UCP1 is indeed expressed only in brown adipose tissus [Bouilland et al., Proc. Natl. Acad. Sci., 82:445-448 (1985); Jacobsson et al., J. Biol. Chem., 260:16250-16254 (1985)]. Genetic mapping studies have shown that the human UCP1 gene is located on chromosome 4. [Cassard et al., J. Cell. Biochem., 43:255-264 (1990)].

Another human UCP, referred to as UCPH or UCP2, has also been described. [Gimeno et al., Diabetet, 30 46:900-906 (1997); Flemy et al., Nat. Genct., 15:269-272 (1997); Boss et al., FEBS Letters, 408:39-42 (1997); see also, Wolf, Nur. Rev., 55:178-179 (1997)]. Flemy et al. teach that the UCP2 protein has 59% amino acid identity to UCP1, and that UCP2 maps to regions of human chromosome 11 which have been linked to hyperiusulinaemia and obesity. [Flemy et al., supra]. It has also been reported that UCP2 is expressed in a variety of adult tissues, such as brain and muscle and fat cells. [Gimeno et al., supra, and Flemy et al., supra].

35 A third human UCP, UCP3, was recently described in Boss et al., supra: Vidal-Pulg et al., Blochem. Biophys. Res. Comm., 235:79-82 (1997); Solanes et al., J. Biol. Chem., 272:25433-25436 (1997); and Gong et al., J. Biol. Chem., 272:24129-24132 (1997). [See also Great Britain Patent No. 9716886]. Solanes et al.

report that unlike UCP1 and UCP2, UCP3 is expressed preterentially in human skeleral muscle, and that the UCP3 gene maps to human chromosome 11, adjacem to the UCP2 gene. [Solanes et al., supra]. Gong et al. describe that the UCP3 expression can be regulated by known thermogenic stimuli, such as thyroid hormone, beta3-andrenergic agonists and teptin. [Gong et al., supra].

HY PROPE

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Efforts are being undertaken by both industry and academia to identify new, native transmembrane proteins. Many efforts are focused on the serecting of mammalian recombinated DNA libraries to identify the coding sequences for novel transmembrane proteins. We berein describe the identification and characterization of a novel transmembrane protein designated berein as PRO193.

120. PKO113

Polypeptides such as the human 2-19 protein may function as cytokines. Cytokines are low molecular weight proteins which function to stimulate or inhibit the differentiation, proliferation or function of immune cells. Cytokine proteins often act as intercellular messengers and have multiple physiological effects. Given the physiological importance of immune mechanisms in vivo, efforts are currently being undertaken to identify new, native proteins which are involved in effecting the immune system. We describe herein the identification of a novel polypeptide which has sequence similarity to the human 2-19 protein.

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121. PRO1338

Carbonic anhydrase is an exaymatic protein that which aids carbon dioxide transport and release in the mammalian blood system by catalyzing the synthesis (and the dehydration) of carbonic acid from (and to) carbon dioxide and water. Thus, the actions of carbonic anhydrase are essential for a variety of important physiological reactions in the mammal. As such, there is significant interest in the identification and characterization of novel polypeptides having homology to carbonic anhydrase. We herein describe the identification and characterization of novel polypeptides having homology to carbonic anhydrase, designated herein as PRO 1335 polypeptides.

122. PRO1329

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins.

Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel accreted proteins. We herein describe the identification and characterization of a novel secreted protein designated berein as PRO1329.

123. PRO1550

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins.

35 Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. We herein describe the identification and characterization of a novel secreted protein designated herein as PRO1550.

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SUMMARY OF THE INVENTION

PRO1560

A cDNA clone (DNA19902-1669) has been identified that encodes a novel polypeptide believed to be a novel member of the tetraspan family, designated in the present application as "PRO1560."

In one embodiment, the invention provides an isolated meleic acid molecule comprising DNA encoding RO1560 polypeptide.

In one aspect, the isolated nucleic usual comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1560 polypeptide having the sequence of amino acid residues from 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1560 polypeptide comprising DNA hybridizing to the complement of the nucleic acid hetween about residues 167 and about 775, inclusive, of Figure 1 (SEQID NO:3). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203454 (DNA19902-1669), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic 20 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203454 (DNA19902-1669).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypepuide having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence 25 identity to the sequence of amino acid residues from about 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1560 polypoptide having the sequence of 30 amino acid residues from about 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about as 80% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding 35 a PRO1560 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position

I through about amino acid position 42 in the sequence of Figure 2 (SEQ ID NO:4). The transmembrane domains have been tentatively identified as at about amino acid positions 19-42, 61-83, 92-114 and 209-230 in the PRO1560 amino acid sequence (Figure 2, SEQ ID NO:4).

In another aspect, the invention concerns an toolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, most preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1560 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1560 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO 1560 polypeptide, which in one embodiment, includes an amino acid acquence comprising residues 1 or about 43 through 245 of Figure 2 (SEQ ID NO:4).

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In another aspect, the invention concerns an isolated PRO1560 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4).

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In a further expect, the invention concerns an isolated PRO1560 polypeptide, comprising an amino acid sequence exercing at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 43 through 245 of Figure 2 (SEQ ID NO:4).

25 In yet another aspect, the invention concerns an isolated PRO1560 polypeptide, comprising the sequence of amino acid residues 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4), or a fragment thereof sufficient to provide a binding site for an anti-PRO1560 antibody. Preferably, the PRO1560 fragment retains a qualitative binlogical activity of a native PRO1560 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

30 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1560 polypeptide having the
sequence of amino acid residues from about 1 or about 43 to about 245, inclusive of Figure 2 (SEQ ID NO:4),
or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell
sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (iii) culturing a host cell
comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii)
recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and aniagonists of a native PRO1560

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polypoptide. In a particular embodiment, the agonist or aniagonist is an anti-PRO1560 antibody

In a further embodiment, the invention concerns a method of identifying agouists or antagonists of a native PRO1560 polypeptide, by contacting the native PRO1560 polypeptide with a candidate molecule and monitoring a hiological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1560 polypeptide, or an agonist or autogenist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

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PRO444

A cDNA clone (DNA26846-1393) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO444."

10 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO444 polypeptide. . .

In one aspect, the isolated aucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule executing a PRO444 polypeptide having the sequence of amino acid residues from about 1 or about 17 to about 117, inclusive of Figure 4 (SBQ ID).

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NO:6), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated modele acid molecule encoding a PRO444 polypeptide comprising DNA hybridizing to the complement of the medeic acid between about residues 656 and about 958, inclusive, of Figure 3 (SEQ ID NO:5). Preferably, hybridization occurs under stringent hybridization and weath conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule canceling the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203406:

25 (DNA26846-1397), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203406 (DNA26846-1397).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence 30 identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, to the sequence of amino acid residues from about 1 or about 17 to about 117, inclusive of Figure 4

(SEQ ID NO:6), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 10 nucleotides, more preferably at least about 20 nucleotides, and most preferably at least about 40 nucleotides and 35 produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO444 polypeptide having the sequence of amino acid residues from about 17 or about 17 to about 117, inclusive of Figure 4 (SEQ ID NO:5), or (b) the complement of the DNA molecule of (a), and, if the DNA

molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an invlated nucleic acid molecule comprising DNA encoding a PRO444 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding mucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position i through about amino acid position 16 in the sequence of Figure 4 (SEQ ID NO:6).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scuring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 17 to about 117, inclusive of Figure 4 (SEQ ID NO:5), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO444 polypeptide coding sequence that may find use as tybridization probes. Such mucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides tsolated PRO444 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO444 polypeptide, which in one combodiment, includes an amino acid sequence comprising residues 1 or about 17 to 117 of Figure 4 (SEQ ID NO:6).

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In another aspect, the invention concerns an isolated PRO444 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, more preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 17 to about 117, inclusive of Figure 4 (SEQ ID NO:6).

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In a further aspect, the invention concerns an isolated PRO444 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 17 to 117 of Figure 4 (SEQ ID NO:6).

30 In yet another aspect, the invention connerns an Isolated PRO444 polypeptide, comprising the sequence of amino acid residues 1 or about 17 to about 117, inclusive of Figure 4 (SEQ ID NO:6), or a fragment thereof sufficient to provide a binding site for an anti-PRO444 antibody. Preferably, the PRO444 fragment retains a qualitative biological activity of a native PRO444 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA solicente under stringent conditions with (a) a DNA molecule encoding a PRO444 polypeptide having the sequence of amino acid residues from about 10 r about 117, inclusive of Figure 4 (SEQ ID NO:6), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80%

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sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

3. PROIDI

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A cDNA clone (DNA56107-1415) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1018".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

- 10 In one aspect, the isolated modeic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule encoding a PRO1018 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8), or (b) the complement of the DNA molecule of (a).
- In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1018 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 129 or about 201 and about 695, inclusive, of Figure 5 (SEQ ID NO:7). Preferably, hybridization occurs under stringent bybridization and wash conditions.
- In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having
 20 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule
 emodding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203405
 (DNA56107-1415) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the
 mucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in
 ATCC Deposit No. 203405 (DNA56107-1415).

In still a further aspect, the invention concerns an isolated mucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, to the sequence of amino acid residues 1 or about 25 to about 189, inclusive of Figure62 (SBQ ID NO:8), or (b) the complement of the DNA of (s).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1018 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8), or (b) the complement of the DNA molecule of (a), and, if

35 the DNA molecule has at least about an 80 % sequence identity, preferrably at least about an 85% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity, on the preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA exceeding a PRO1018 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 24 in the sequence of Figure 6 (SEQ ID NO:8). The transmembrane domains have been tentatively identified as extending from about amino acid position 86 to about amino acid position 103 and from about amino acid position 60 to about amino acid position 75 in the PRO1018 amino acid sequence (Figure 6, SEQ ID NO:8).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 83% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid acqueence of residues 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1018 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence abown in Figure 5 (SEQ ID NO:7).

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In another embodiment, the invention provides isolated PRO1018 polypeptide encoded by any of the isolated medicio acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1018 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 25 to about 189 of Figure 6 (SEQ ID NO:8).

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In another aspect, the invention concerns an isolated PRO1018 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8).

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In a further aspect, the invention concerns an isolated PRO1018 polypoptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8).

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In yet another aspect, the invention concerns an isolated PRO1018 polypeptide, comprising the sequence of amino acid residues 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8), or a fragment thereof sufficient to provide a binding site for an anti-PRO1018 antibody. Preferably, the PRO1018 fragment retains a qualitative biological activity of a native PRO1018 polypeptide.

35 In a still further expect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1018 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 189, inclusive of Figure 6 (SEQ ID NO:8),

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or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 83% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

i. PRO177

A cDNA clone (DNA56406-1704) has been identified, having homology to nucleic acid encoding a retinol dehydrogenase protein that encodes a novel polypeptide, designated in the present application as "PRO1773".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1773 polypoptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1773 polypeptide having 15 the sequence of amino acid residues from about 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1773 polypeptide comprising DNA hybridizing to the complement of the modelic acid between about nucleotides 111 or about 162 and about 1667, inclusive, of Figure 7 (SEQ ID NO:9). Preferably, hybridization occurs under stringent hybridization and wash conditions.

NO:10), or (b) the complement of the DNA molecule of (a).

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In a further aspect, the invention concerns an isolated mucleic acid molecule comprising DNA having at least about 80% sequence identity, most preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203478

25 (DNA56406-1704) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203478 (DNA56406-1704).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 525 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (s) a DNA 55 molecule encoding a PRO1773 polypeptide having the sequence of amino acid restdutes from 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10), or (b) the complement of the DNA molecule of (s), and, if the DNA molecule has at least about an 80% sequence identity, prefereably at least about an 85% sequence

identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1773 polypeptide, with or without the N-terminal signal sequence and/or the initiating methicaine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or it complementary to such encoding models acid molecule. The signal peptide has been transively identified as extending from about amino acid position 1 or about amino acid position 17 in the sequence of Figure 8 (SEQ ID NO:10). The transmembrane domain has been tentatively identified as extending from about amino acid position 135 in the PRO1773 amino acid sequence (Figure 8, SEQ ID NO:10).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the armino acid sequence of residues 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1773 polypeptide coding sequence that may find

15 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 7 (SEQ ID NO.9).

In another embodiment, the invention provides isolated PRO1773 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

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In a specific aspect, the invention provides isolated native sequence PRO1773 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues I or about 18 to about 319 of Figure 8 (SEQ ID NO:10).

In another aspect, the invention concerns an isolated PRO1773 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10).

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In a further expect, the invention concerns an isolated PRO1773 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, mont preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10).

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In yet another aspect, the invention concerns an isolated PRO1773 polypeptide, comprising the acquence of amino acid residues I or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10), or a fragment thereof sufficient to provide a binding site for an ani-PRO1773 antibody. Preferably, the PRO1773 fragment retains a qualitative biological activity of a native PRO1773 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1773 polypeptide having the

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sequence of amino acid residues from about 1 or about 18 to about 319, inclusive of Figure 8 (SEQ ID NO:10), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1773 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1773 antibody.

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In a further embodiment, the invention concerns a method of identifying agonists or anagonists of a native PRO1773 polypeptide by contacting the native PRO1773 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO1773 polypeptide, or an agonist or annagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

PR01477

A cDNA clone (DNA56529-1647) has been identified, having homology to nucleic acid encoding mannosidase protein that encodes a novel polypopide, designated in the present application as 'PRO1477'.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO 1477 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1477 polypeptide having the sequence of amino acid residues from about 1 to about 659, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1477

25 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 23 and about 2119, inclusive, of Figure 9 (SEQ ID NO:11). Perferably, hybridization occurs under stringent bybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identily, preferably at least about 85% sequence identily, most preferably at least about 95% sequence identily to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203293 (DNA56529-1647) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203293 (DNA56529-1647).

35 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, more preferably at least about 95% sequence.

identity to the sequence of amino acid residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA of (a).

In a further expect, the invention concerns an isolated nucleic acid molecule having at least \$40 nucleotides and produced by hybridizing a test DNA molecule under stringern conditions with (a) a DNA molecule encoding a PRO1477 polypeptide having the sequence of amino acid residues from 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about as 80 % sequence identity, prefereably at least about as 85 % sequence identity, more preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

10 a PRO1477 polypeptide, with or without and/or the initiating methionine, and its soluble, i.e., transmembrane
domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The
transmembrane domains have been tentatively identified as extending from about amino acid position 21 to about
amino acid position 40 and from about amino acid position 84 to about amino acid position 105 in the PRO1477
amino acid sequence (Figure 10, SEQ ID NO:12).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 80% positives, more preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA of (a).

20 Another embodiment is directed to fragments of a PRO1477 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 9 (SEQ ID NO:11).

25 In another embodiment, the invention provides isolated PRO1477 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1477 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 699 of Figure 10 (SEO ID NO:12).

30 In another aspect, the invention concerns an isolated PRO1477 pulypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12).

In a further aspect, the invention concerns an isolated PRO1477 polypeptide, comprising an amino acid

55 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12).

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In yet another aspect, the invention concerns an isolated PRO1477 polypeptide, comprising the sequence of antino acid residues 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or a fragment thereof sufficient to provide a binding site for an anti-PRO1477 antibody. Preferably, the PRO1477 fragment retains a qualitative biological activity of a native PRO1477 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA solutions under stringent conditions with (a) a DNA molecule encoding a PRO1477 polypeptide having the sequence of smino acid residues from about 1 to about 699, inclusive of Figure 10 (SEQ ID NO:12), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 80% sequence identity, more preferably at least about a 80% sequence identity to (a) or (b), (ii) culturing a bost cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the

polypopide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1477

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1477 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a mative PRO1477 polypeptide by contacting the native PRO1477 polypeptide with a candidate molecule and

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In a still further embodiment, the invention concerns a composition comprising a PRO1477 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

monitoring a biological activity mediated by said polypeptide.

20 6. PRO1478

A cDNA clone (DNA56531-1648) has been identified that encodes a novel polypeptide having sequence identity with galactosyltransferase and designated in the present application as "PRO1478."

In one embodiment, the inversion provides an isolated nucleic acid molecule comprising DNA encoding a PRO1478 polypeptide.

25 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1478 polypepide having the sequence of amino acid residues from about 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or (b) the complement of the DNA molecule of (a).

30 In snother aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1478 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 77 and about 1057, Inclusive, of Figure 11 (SEQ ID NO:16). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having
35 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule
encoting the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203286

(DNA56531-1648), or (b) the complement of the DNA molecule of (s). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203286 (DNA56531-1648).

In a still further aspect, the inversion concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1478 polypepoide having the sequence of amino acid resistates from about 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, most preferably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1478 polypeptide in its soluble form, i.e. transmembrane domain detered or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domain (type II) has been tentatively identified as extending from about amino acid position 29 through about amino acid position 49 in the PRO1478 amino acid sequence (Figure 12, SEQ ID NO:17). Therefore, a peptide including amino acids 50-227, with or without amino acids 1-28, is specifically embodied berein, as well as the nucleic acid encoding such a peptide.

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1478 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1478 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

in a specific aspect, the invention provides isolated native sequence PRO1478 polypopride, which in one embodiment, includes an amino acid sequence comprising residues 1 through 327 of Figure 12 (SEQ ID NO:17).

In another aspect, the invention concerns an isolated PRO1478 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the

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sequence of amino acid residues 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17)

In a further aspect, the invention concerns an isolated PRO1478 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 80% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 1 through 327 of Figure 12 (SEQ ID NO:17).

In yet another aspect, the invention concerns an isolated PRO1478 polypeptide, comprising the sequence of amino acid residues 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or a fragment thereof sufficient to provide a binding site for an anti-PRO1478 antibody. Preferably, the PRO1478 fragment retains a qualitative biological activity of a native PRO1478 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA
10 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1478 polypeptide having the
sequence of amino acid residues from about 1 to about 327, inclusive of Figure 12 (SEQ ID NO:17), or (b) the
complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence
identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising
15 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1478 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1478 antibody.

polypeptide from the cell culture.

In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a 20 native PRO1478 polypeptide, by contacting the native PRO1478 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1478 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

25 7. PRO831

A cDNA clone (DNA56862-1343) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO831".

In one embodiment, the invention provides an isolated nucleic acid molecute comprising DNA encoding a PRO831 polypepside.

- 30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO831 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22), or (b) the complement of the DNA molecule of (a).
- 35 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO831 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 40 or about 85 and about 238, inclusive, of Figure 13 (SEQ ID NO:21). Preferably, hybridization occurs under

stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203174 (DNA56862-1343) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203174 (DNA56862-1343).

In still a further aspect, the invention concerns an itolated nucleic acid molecule comprising (a) DNA exceeding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 470 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule emcoding a PRO831 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 85% sequence identity, preferrably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO831 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been remainvely identified as extending from about amino acid position 1 to about amino acid position 15 in the sequence of Figure 14 (SEQ ID NO:22).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO831 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 13 (SEQ ID NO.21).

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In another embodiment, the invention provides isolated PRO831 polypeptide encoded by any of the isolated nucleic acid sequences hereinabuve identified.

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In a specific aspect, the invention provides isolated native sequence PRO831 polypeptide, which in

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certain embodiments, includes an amino acid sequence comprising residues 1 or about 16 to about 73 of Figure 14 (SEQ ID NO:22).

In another aspect, the invention concerns an isolated PRO831 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO.22).

In a further aspect, the invention concerns an isolated PRO831 polypeptide, comprising an ambo acid sequence enoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives when compared with the amino acid sequence of residues 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22).

In yet another aspect, the invention concerns an isolated PRO831 polypepitie, comprising the sequence of amino acid residues 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22), or a fragment thereof sufficient to provide a binding site for an anti-PRO831 antibody. Preferably, the PRO831 fragment retains a qualitative biological activity of a native PRO831 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO831 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 73, inclusive of Figure 14 (SEQ ID NO:22), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

PROLLIS

A cDNA clone (DNAS7254-1477) has been identified that encodes a novel polypeptide having sequence 25 identity with leucine rich repeat proteins and designated in the present application as "PRO1113."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1113 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encouling a PRO1113 polypeptide having the sequence of amino acid residues from about 1 to about 516, inclusive of Figure 16 (SEQ ID NO:24), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule emoding a PRO1113 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 214 and 35 about 2061, inclusive, of Figure 15 (SEQ ID NO:23). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203289 (DNA57254-1477), or (b) the complement of the DNA molecule of (a). In a preferred enthodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203289 (DNA57254-1477).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA cancoding a polypoptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 616, inclusive of Figure 16 (SEQ ID NO.24), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1113 polypeptide having the sequence of amino acid residues from about 1 to about 616, inclusive of Figure 16 (SEQ ID NO:24), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity of (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1113 polypeptide in its soluble, i.e. transmembrane domain deleted or inactivated variants, or is 20 complementary to such encoding nucleic acid molecule. The transmembrane domain has been tentatively identified as extending from about amino acid position 13 through about amino acid position 40 in the PRO1113 amino acid sequence (Figure 16, SEQ ID NO:24). Thus, also presented herein is a peptide comprising amino acids 41-516, and optionally 1-12 of SEQ ID NO:24, and the nucleic acids encoding the same.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

25 cacoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
amino acid sequence of residues 1 to about 616, inclusive of Figure 16 (SEQ ID NO:24), or (b) the complement
of the DNA of (a).

Another embodiment is directed to fragments of a PRO1113 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1113 polypeptide encoded by any of the

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In another embodiment, the invention provides isolated PRO1113 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1113 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 616 of Figure 16 (SEQ ID NO:24).

In another aspect, the invention concerns an isolated PRO1113 polypeptide, comprising an amino acid

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sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to the preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 616, inclusive of Figure 16 (SEQ ID NO.24).

In a further aspect, the invention concerns an isolated PRO1113 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of fresidues 1 through 616 of Figure 16 (SEQ ID NO:24).

In yet amother aspect, the invention concerns an isolated PRO1113 polypeptide, comprising the sequence of amino acid residues 1 to about 616, inclusive of Figure 16 (SEQ ID NO.24), or a fragment thereof sufficient to provide a binding site for an ami-PRO1113 amibody. Preferably, the PRO1113 fragment retains a qualitative 10 biological activity of a native PRO1113 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1113 polypeptide having the sequence of amino acid residues from about 1 to about 616, inclusive of Figure 16 (SEQ ID NO:24), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1113

20 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1113 amthody.

In a further embodiment, the invention concerns a method of identifying agonists or anagonists of a native PRO1113 polypeptide, by contacting the mative PRO1113 polypeptide with a emdidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1113 polypeptide.

25 or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable currier.

PRO1194

A cDNA clone (DNA57841-1522) has been identified that encodes a novel scoreted polypeptide designated in the present application as "PRO1194."

30 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA exceeding a PRO1194 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1104 polypeptide having the sequence of amino acid residues from 1 or about 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1194

polypeptide comprising DNA hybridizing to the complement of the nucleit acid between about residues 72 and about 251, inclusive, of Figure 17 (SEQ ID NO.28). Preferably, hybridization occurs under stringent hybridization and wash conditions.

in a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203458 (DNA57841-1522), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203458 (DNA57841-1522).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1194 polypeptide having the sequence of annho acid residues from about 22 to about 81, inclusive of Figure 18 (SEQ ID NO.29), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1194 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1194 polypeptide encoded by any of the isolated nucleic acid sequences bereimshove defined.

In a specific aspect, the invention provides isolated native sequence PRO1194 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 22 through 81 of Figure 18 (SEQ ID NO.29).

In another sepect, the invertion concerns an isolated PRO1194 polypepide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity in the preferably at least about 95% sequence identity to the

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sequence of amino acid residues 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29).

In a further aspect, the invention concerns an isolated PRO1194 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 80% positives, more preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 22 through 81 of Figure 18 (SEQ ID NO.29).

In yet another aspect, the invention concerns an isolated PRO1194 polypeptide, comprising the sequence of amino acid residues 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29), or a fragment thereof sufficient to provide a binding site for an anti-PRO1194 antibody. Preferably, the PRO1194 fragment retains a qualitative biological activity of a native PRO1194 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) bybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1194 polypeptide having the scquence of amino acid residues from about 22 to about 81, inclusive of Figure 18 (SEQ ID NO:29), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 80% sequence identity, more preferably at least about a 80% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising to the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and amagonists of a native PRO1194 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1194 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a 20 maive PRO1194 polypeptide, by contacting the native PRO1194 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1194 polypopide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

10. PROLLIG

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A cDNA clone (DNAS8727-1474) has been identified, having homology to nucleic acid encoding myeloid upregulated protein that encodes a novel polypeptide, dealgnated in the present application as "PRO1110".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding 30 a PRO1110 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1110 polypeptide having the sequence of amino acid residues from about 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1110 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleorides 131

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and about 1096, inclusive, of Figure 19 (SEQ ID NO.30). Preferably, hybridization occurs under stringent bybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203171 (DNA58727-1474) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203171 (DNA58727-1474).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule traving at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1110 polypeptide having the sequence of amino acid residues from 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1110 polypoptide, with or without the initiating methionine and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains have been tentatively identified as extending from about amino acid position 41 to about amino acid position 60, from about amino acid position 60, from about amino acid position 101 to about amino acid position 120, from about amino acid position 137 to about amino acid position 121 to about amino acid position 125 to about amino acid position 255, and from about amino acid position 256, from about amino acid position 255, and from about amino acid position 254 to about amino acid position 254 to about amino acid position 254 to about amino acid position 257.

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 90% positives when compared with the amiho acid sequence of residues I to about 922, inclusive of Figure 20 (SEQ ID NO:31), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1110 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,

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preferably from about 20 to about 60 mecleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 19 (SEQ ID NO:30).

In another embediment, the invention provides isolated PRO1110 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1110 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 322 of Figure 20 (SEQ ID NO.31).

In another aspect, the invention concerns an isolated PRO1110 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more 10 preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31).

In a further aspect, the invention concerns an isolated PRO1110 polypeptide, comprising an amino acid sequence ecoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 90% positives when compared with the amino acid sequence of residues 1 to about 322, inclusive of Figure 20 (SEQ ID NO.31).

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In yet another aspect, the invention concerns an isolated PRO1110 polypeptide, comprising the sequence of amino acid residues 1 to about 322, inclusive of Figure 20 (SEQ ID NO:31), or a fragment thereof sufficient to provide a binding site for an ami-PRO1110 amibody. Preferably, the PRO1110 fragment retains a qualitative biological activity of a native PRO1110 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1110 polypeptide having the sequence of amino acid residues from about 1 to about 322, inclusive of Figure 20 (SEQ ID NO.31), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1110 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1110 antibody.

30 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1110 polypeptide by contacting the native PRO1110 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1110 polypeptide or an agonist or amagonist as hereinabove defined, in combination with a pharmaceutically acceptable currier

11. PRO1378

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A cDNA clone (DNA58730-1607) has been identified that encodes a novel secreted polypeptide

designated in the present application as "PRO1378".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1378 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1378 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 335, inclusive of Figure 22 (SEQ ID NO:33), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1378 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 1365 and about 2369, inclusive, of Figure 21 (SEQ ID NO:32). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203221 (DNA58730-1607), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203221 (DNA58730-1607).

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

20 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
identity to the sequence of amino acid residues from 1 or about 16 to about 335, inclusive of Figure 22 (SEQ

1D NO:33), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 20 nucleotides, preferably at least about 50 nucleotides, and more preferably at least about 100 nucleotides and produced by bybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1378 polypeptide having the sequence of amino acid residues from about 16 to about 335, inclusive of Figure 22 (SEQ ID NO:33), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated meteic acid molecule comprising DNA encoding a PRO1378 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding mucleic acid molecule. The signal peptide has been tentarively identified as extending from amino acid position I through about amino acid position 15 in the sequence of Figure 22 (SEQ ID NO:33).

In another aspect, the invention concerns an isolated muleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more

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preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to about 335, inclusive of Figure 22 (SEQ ID NO:33), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1378 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 medentides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50

In another embodiment, the invention provides isolated PRO1378 polypeptide encoded by any of the isolated nucleic acid sequences bereinabove defined.

nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In a specific aspect, the invention provides isolated tative sequence PRO1378 polypeptide, which in one
10 embodiment, includes an amino acid sequence comprising residues 16 to 335 of Figure 22 (SEQ ID NO:33),
10 another aspect, the invention concerns an isolated PRO1378 polypeptide, comprising an amino acid

In another speet, the invention concerns an isolated PRO1378 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to the sequence of amino acid residues 16 to about 335, inclusive of Figure 22 (SEQ ID NO.335).

15 In a further aspect, the invention concerns an isolated PRO1378 polypoptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 83% positives, more preferably at least about 90% positives, most preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to 335 of Figure 22 (SEQ ID NO:33).

In yet another aspect, the invention concerns an isolated PRO1378 polypeptide, comprising the sequence
20 of amino actit residuces 16 to about 335, inclusive of Figure 22 (SEQ ID NO:33), or a fragment thereof sufficient
to provide a binding site for an ami-PRO1378 antibody. Preferably, the PRO1378 fragment retains a qualitative
biological activity of a native PRO1378 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) bybridizing a rest DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1378 polypeptide having the sequence of amino acid residues from about 16 to about 335, inclusive of Figure 22 (SEQ ID NO:33), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 83% sequence identity, more preferably at least about an 83% sequence identity to (a) or (b), (ii) enturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

12. PRO1481

A cDNA clone (DNAS8732-1650) has been identified that encodes a novel polypeptide designated in the present application as "PRO1481."

35 In one embodiment, the invention provides an isolated muleic acid molecule comprising DNA encoting a PRO1481 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity

or (b) the complement of the DNA molecule of (a). the sequence of amino acid residues from 1 or about 24 to about 334, inclusive of Figure 24 (SEQ ID NO:41) preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1481 polypoptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, mos

polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 88 and hybridization and wash conditions. about 1321, inclusive, of Figure 23 (SEQ ID NO:40). Preferably, hybridization occurs under stringent In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1481

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about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule Deposit No. 203290 (DNA58732-1650). acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC (DNA58732-1650), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203290 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA baving

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15 NO:41), or the complement of the DNA of (a). encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity to the sequence of amino acid residues from about 24 to about 334, inclusive of Figure 24 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DN!

at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably unino acid residues from about 24 to about 334, inclusive of Figure 24 (SEQ ID NO:41), or (b) the complement under stringent conditions with (a) a DNA molecule encoding a PRO1481 polypeptide having the sequence of In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

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encoding nucleic acid molecule. The signal peptide has been ternatively identified as extending from amino acid its soluble, i.e. transmembrane domain deleted, truncated or inactivated variants, or is complementary to such a PRO1481 polypeptide, with or without the N-cerminal signal sequence and/or the initiating methiomine, and about amino acid position 262 in the PRO1481 amino acid sequence (Figure 24, SEQ ID NO:41). position I through about amino acid position 23 in the sequence of Figure 24 (SEQ ID NO:41). The transmembrane domain has been tentatively identified as extending from about amino acid position 235 through In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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35 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 24 to about 334, inclusive of Figure 24 (SEQ ID NO:41), or (b) the complement In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DN/

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of the DNA of (a)

preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length Another embodiment is directed to fragments of a PRO1481 polypeptide coding sequence that may find

isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated PRO1481 polypeptide encoded by any of the

embodiment, includes an amino acid sequence comprising residues 24 through 334 of Figure 24 (SEQ ID In a specific aspect, the invention provides isolated native sequence PRO 1481 polypeptide, which in one

10 sequence of amino acid residues 24 to abour 334, inclusive of Figure 24 (SEQ ID NO:41). preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more In another aspect, the invention concerns an isolated PRO1481 polypeptide, comprising an amino acid

5 sequence scoring at least about 80 % positives, preferably at least about 85 % positives, more preferably at least of residues 24 through 334 of Figure 24 (SEQ ID NO:41). about 90% positives, most preferably at least about 95% positives when compared with the unino acid sequence In a further aspect, the invention concerns an isolated PRO1481 polypeptide, comprising an amino acid

20 to provide a binding site for an anti-PRO1481 antibody. Preferably, the PRO1481 fragment retains a qualitative biological activity of a native PRO1481 polypeptide. of amino axid residues 24 to about 334, inclusive of Figure 24 (SEQ ID NO:41), or a fragment thereof sufficient In yet another aspect, the invention concerns an isolated PRO1481 polypeptide, comprising the sequence

23 the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence sequence of amino acid residues from about 24 to about 334, inclusive of Figure 24 (SEQ ID NO:41), or (b) molecule under stringent conditions with (a) a DNA molecule encoding a PRO1481 polypeptide having the In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

polypepiide from the cell culture. the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most proferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising

30 polypeptide. In a particular embodiment, the aganist or antagonist is an anti-PRO1481 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1481

native PRO1481 polypeptide, by contacting the native PRO1481 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide. In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a

ઝ or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO1481 polypeptide

13. PRO1189

A cDNA clone (DNA58828-1519) has been identified that encodes a novel polypeptidehaving homology to E25 which is designated in the present application as "PRO1189."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO 1189 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA nuclecule encoding a PRO1189 polypeptide having the sequence of amino acid residues from about 1 to about 263, inclusive of Figure 26 (SEQ ID NO:43), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1189 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 79 and about 867, inclusive, of Figure 25 (SEQ ID NO:42). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mantre polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203172 (DNA58828-1519), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the meleic acid comprises a DNA encoding the same mantre polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203172 (DNA58828-1519).

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA exceeding a polypeptide having at least about 80% sequence identity, preferably at least about 95% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 263, Inclusive of Figure 26 (SEQ ID NO:43), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic ucid molecule having at least about 50 mucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1189 polypeptide having the sequence of amino acid residues from about 1 to about 263, inclusive of Figure 26 (SEQ ID NO:43), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about an 80% sequence identity of (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1189 polypeptide with its transmembrane domain deteted or inactivated, or is complementary to such 35 encoding nucleic acid molecule. The transmembrane domain has been tentatively identified as extending from about amino acid position 53 through about amino acid position 75 in the PRO1189 amino acid sequence (Figure 26, SEQ 1D NO:43).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide acoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 263, inclusive of Figure 26 (SEQ ID NO:43), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1189 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1189 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

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In a specific aspect, the invention provides isolated native sequence FRO1189 polypoptics, which in one cambodiment, includes an antino acid sequence comprising residues 1 to 263 of Figure 26 (SEQ ID NO:43).

In another aspect, the invention concerns an isolated PRO1189 polypoptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 263, inclusive of Figure 26 (SEQ ID NO;43).

In a further aspect, the inversion concerns an isolated PRO1189 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid requence 20 of residues 1 to 263 of Figure 26 (SEQ ID NO:43).

In yet another aspect, the invention concerns an isolated PRO1189 polypeptide, comprising the sequence of amino acid residues 1 to about 263, inclusive of Figure 26 (SEQ ID NO:43), or a fragment thereof sufficient to provide a binding site for an anti-PRO1189 antibody. Preferably, the PRO1189 fragment retains a qualitative biological activity of a native PRO1189 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1189 polypeptide having the sequence of amino acid residues from about 1 to about 263, inclusive of Figure 26 (SEQ ID NO:43), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 80% sequence identity, more preferably at least about a 80% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1189 polypeptide. In a particular embodiment, the agonist or artagonist is an arti-PRO1189 antibody.

35 In a further embodiment, the invention concerns a method of identifying agonists or anagonists of a native PRO1189 polypeptide, by contacting the native PRO1189 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO | 189 polypeptide or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

PR01416

A cDNA clone (DNAS8852-1637) has been identified that encodes a novel polypeptide, designated in the present application as "PRO1415".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding RO1415 polypepide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1415 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1415 polypeptide comprising DNA hybridizing to the complement of the mucleic acid between about nucleotida 148 or about 223 and about 996, inclusive, of Figure 27 (SEQ ID NO:49). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated markeic axid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203271 (DNAS8852-1637) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the inveleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203271 (DNAS8852-1637).

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In still a further appear, the invention concerns an isolated nucleic acid molecule comprising (a) DNA crecoting a polypeptide having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, one preferably at least about 90% sequence identity, one preferably at least about 95% sequence identity, on the sequence of amino acid residues 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule excoding a PRO1415 polypeptide having the sequence of amino acid residues from 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the est DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1415 polypoptide, with or without the N-terminal signal sequence and/or the initiating methionine, and

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its soluble, i.e., transmembrane domain deleted or inacrivated variants, or is complementary to such encoding nutricic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 25 in the sequence of Figure 28 (SEQ ID NO:50). The transmembrane domain has been tentatively identified as extending from about amino acid position 94 to about amino acid position 118 in the PRO1415 amino acid sequence (Figure 28, SEQ ID NO:50).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide ecoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1415 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and may be derived from the nucleotide in length and may be derived from the nucleotide sequence shown in Figure 27 (SEQ ID NO:49).

15 In another embodiment, the invention provides isolated PRO1413 polypeptide encoded by may of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1415 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 26 to about 283 of Figure 28 (SEQ ID NO:50).

In another aspect, the invention concerns an isolated PRO1415 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to the sequence of amino acid residues 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50).

In a further aspect, the invention concerns an isolated PRO 1415 polypeptide, comprising an amino acid

25 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least
about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence
of residues 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50).

Layet another aspect, the invention concerns an isolated PRO1415 polypeptide, comprising the sequence of amino acid residues 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID NO:50), or a fragment 30 thereof sufficient to provide a binding site for an anti-PRO1415 antibody. Preferably, the PRO1415 fragment retains a qualitative biological activity of a native PRO1415 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1415 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 283, inclusive of Figure 28 (SEQ ID 35 NO:50), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about an 95% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a bost cell

comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1415 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1415 amibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1415 polypeptide by contacting the maive PRO1415 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1415 polypeptide, or an agonist or amagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier,

10 IS. PRO1411

A cDNA close (DNA59212-1027) has been identified that encodes a novel secreted polypopide designated in the present application as "PRO1411."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding RO1411 polypernide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1411 polypeptide having the sequence of amino acid residues from 1 or about 22 to about 440, inclusive of Figure 30 (SEQ ID NO:52), or (b) the complement of the DNA molecule of (a).

20 In another sepect, the invention concerns an isolated nucleic acid molecule emoding a PRO1411 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 247 and about 1503, inclusive, of Figure 29 (SEQ ID NO:51). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having 25 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203245 (DNA59212-1627), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the molecule comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203245 (DNA59212-1627).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 22 to about 440, inclusive of Figure 30 (SEQ ID NO.52), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a text DNA molecule

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under stringent conditions with (a) a DNA molecule encoding a PRO1411 polypeptide having the sequence of antino acid residues from about 22 to about 440, inclusive of Figure 30 (SEQ ID NO.52), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 83% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 22 to about 440, inclusive of Figure 30 (SEQ ID NO:52), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1411 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1411 polypeptide encoded by any of the isolated nucleic neid sequences hereinabove defined.

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In a specific aspect, the invention provides isolated native sequence PRO1411 polypeptide, which in one embodiment, includes an amino acid soquence comprising residues 22 through 440 of Figure 30 (SEQ ID NO.52).

In another aspect, the invention concerns an isolated PRO1411 polypeptide, comprising an amino acid
20 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the
sequence of amino acid residues 22 to about 440, inclusive of Figure 30 (SEQ ID NO:52).

In a further aspect, the invention concerns an isolated PRO1411 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 22 through 440 of Figure 30 (SEQ ID NO:52).

In yet another aspect, the invention concerns an isolated PRO1411 polypeptide, comprising the sequence of amino acid residues 22 to about 440, inclusive of Figure 30 (SEQ ID NO:52), or a fragment thereof sufficient to provide a bluding site for an anti-PRO1411 antibody. Preferably, the PRO1411 fragment retains a qualitative biological activity of a native PRO1411 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) bybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1411 polypeptide having the sequence of amino acid residues from about 22 to about 440, inclusive of Figure 30 (SEQ ID NO:52), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity to (a) or (b), (ii) culturing a bost cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the

polypeptide from the cell culture.

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1411 antibody, In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1411

monitoring a biological activity mediated by said polypeptide native PRO1411 polypeptide, by contacting the native PRO1411 polypeptide with a candidate molecule and In a further embodiment, the invention concerns a method of identifying agorists or antagonists of a

or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier. In a still further embodiment, the invention concerns a composition comprising a PRO1411 polypeptide.

10 designated in the present application as "PRO1295." A cDNA clone (DNAS9218-1559) has been identified that encodes a novel secreted polypeptide

a PRO1295 polypeptide In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

15 preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most or (b) the complement of the DNA molecule of (a). the sequence of amino acid residues from 1 or about 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54), preferably at least about 95 % sequence identity to (a) a DNA molecule encoding a PRO1295 polypeptide having In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 261 and hybridization and wash conditions about 1046, inclusive, of Figure 31 (SEQ ID NO:53). Preferably, hybridization occurs under stringent In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1295

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23 about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least Deposit No. 203287 (DNA59218-1559). acid comprises a DNA encoding the same mature polypepside encoded by the human protein cDNA in ATCC (DNAS9218-1559), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203287 in a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

30 identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence NO:54), or the complement of the DNA of (a). identity to the sequence of amino acid residues from about 19 to about 280, inclusive of Figure 32 (SEQ ID encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence in a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

35 under stringent conditions with (a) a DNA molecule encoding a PRO1295 polypeptide having the sequence of nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

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at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably amino acid residues from about 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54), or (b) the complement

encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more of the DNA of (a) preferably at least about 90% positives, most preferably at least about 95% positives when compared with the arnino acid sequence of residues 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54), or (b) the complement In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

5 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 Another embodiment is directed to fragments of a PRO1295 polypeptide coding sequence that may find

isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated PRO1295 polypeptide encoded by any of the

15 NO:54). embodiment, includes an amino acid sequence comprising residues 19 through 280 of Figure 32 (SEQ ID In a specific aspect, the invention provides isolated native sequence PRO 1295 polypeptide, which in one

20 preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54). sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more In another aspect, the invention concerns an isolated PRO1295 polypeptide, comprising an amino acid

દ્ધ of residues 19 through 280 of Figure 32 (SEQ ID NO:54). about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated PRO1295 polypeptide, comprising an amino acid

to provide a binding site for an ami-PRO1295 antibody. Preferably, the PRO1295 fragment retains a qualitative of amino acid residues 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54), or a fragment thereof sufficient biological activity of a mative PRO1295 polypeptide. In yet another aspect, the invention concerns an isolated PRO 1295 polypeptide, comprising the sequence

30 polypeptide from the cell culture the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the identity, most preferably at least about a 95 % sequence identity to (a) or (b), (ii) culturing a host cell comprising the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence sequence of amino acid residues from about 19 to about 280, inclusive of Figure 32 (SEQ ID NO:54), or (b) identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence molecule under stringent conditions with (a) a DNA molecule encoding a PRO1295 polypeptide having the In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1295 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1295 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1295 polypeptide, by contacting the native PRO1295 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1295 polypoptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

17. PRO135

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A cDNA clone (DNA59219-1613) has been identified that excodes a novel polypeptide having sequence identity with stallytransferases and designated in the present application as "PRO1359" polypeptides.

In one embodiment, the invention provides an isolated nucleit acid molecule comprising DNA encoding RO1359 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1359 polypeptide having the sequence of amino acid residues from 1 or about 32 to about 299, inclusive of Figure 34 (SEQ ID NO.56), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1359 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 277 and about 1080, inclusive, of Figure 33 (SEQ ID NO:55). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further espect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule cucording the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203220 (DNA59219-1613), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203220 (DNA59219-1613).

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In a still further expect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide baving at least about 80% sequence identity, preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of animo acid residues from about 92 to about 299, inclusive of Figure 34 (SEQ ID NO:56), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 30 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1359 polypoptide having the sequence of amino acid residues from about 32 to about 299, inclusive of Figure 34 (SEQ ID NO:56), or (b) the complement

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of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA exceeding a PRO1359 polypeptide in its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domain (type II) has been tentatively identified as extending from about amino acid position 9 through about amino acid position 31 in the PRO1359 amino acid sequence (Figure 34, SEQ ID NO.56).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more 10 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the aminu acid sequence of residues 32 to about 299, inclusive of Figure 34 (SEQ ID NO:56), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1359 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, 15 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1359 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1359 polypeptide, which in one 20 embodiment, includes an amino acid sequence comprising residues 32 through 299 of Figure 34 (SEQ ID NO:56).

In another aspect, the invention concerns an isolated PRO1359 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 32 to about 299, inclusive of Figure 34 (SEQ ID NO:56).

In a further aspect, the invention concerns an isolated PRO 1359 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 32 through 299 of Figure 34 (SEQ ID NO:56).

In yet another aspert, the invention concerns an isolated PRO 1359 polypeptide, comprising the sequence of amino acid residues 32 to about 299, inclusive of Figure 34 (SEQ ID NO:56), or a fragment thereof sufficient to provide a binding site for an anti-PRO 1359 antibody. Preferably, the PRO 1359 fragment retains a qualitative biological activity of a native PRO 1359 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

35 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1359 polypeptide having the
sequence of amino acid residues from about 32 to about 299, inclusive of Figure 34 (SEQ ID NO:56), or (b)
the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence

identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1359 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1359 antibody.

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in a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1359 polypeptide, by contacting the native PRO1359 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1359 polypeptide, or an agonist or amagemist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

PROLLS

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A cDNA clone (DNA59586-1520) has been identified that encodes a novel polypeptide designated in the present application as "PRO1190", and which has homology to CDO protein.

In one embodiment, the invention provides an Isolated nucleic acid molecule comprising DNA encoding a PRO1190 polypeptide.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1190 polypeptide having 20 the sequence of amino acid residues from about 1 to about 1115, inclusive of Figure 36 (SEQ ID NO:58), or (b) the complement of the DNA molecule of (a).

In amother aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1190 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 340 and about 3684, inclusive, of Figure 35 (SEQ ID NO:58). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203288 (DNA59586-1520), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203288 (DNA59586-1520).

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA caccoding a polypeptide having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 1115, inclusive of Figure 36 (SEQ ID NO:58), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1190 polypeptide having the sequence of amino acid residues from about 1105 nuclusive of Figure 36 (SEQ ID NO.58), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, proferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity of (a) or (b), isolating the test DNA molecule.

In a specific espect, the invention provides an isolated nucleic acid molecule comprising DNA exceeding a PRO1190 polypeptide, with one or more of its transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domains have been remaitvely identified in the PRO1190 amino acid sequence shown in Figure 36 (SEQ ID NO:58) as extending from about amino acid position 16 to about amino acid position 30 and from about amino acid position 854 to about amino acid position 879.

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 1115, inclusive of Figure 36 (SEQ ID NO:58), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1190 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, 20 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 50 nucleotides in length, and most preferably from about 40 nucleotides in length.

 In another embodiment, the invention provides isolated PRO1190 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1190 polypopitie, which in one
25 embodiment, includes an amino acid sequence comprising residues 1 to 1115 of Figure 36 (SEQ ID NO:58).

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In another aspect, the invention concerns an isolated PRO1150 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 1115, inclusive of Figure 36 (SEQ ID NO:58).

30 In a further aspect, the invention concerns an isolated PRO1190 polypeptide, comprising an amho acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 1115 of Figure 36 (SEQ ID NO:58).

In yet another aspect, the invention concerns an isolated PRO1190 polypeptide, comprising the sequence of amino acid residues 1 to about 1115, inclusive of Figure 36 (SEQ ID NO:58), or a fragment thereof sufficient to provide a binding site for an anti-PRO1190 antibody. Preferably, the PRO1190 fragment retains a qualitative biological activity of a native PRO1190 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a rest DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1190 polypeptide having the sequence of amino acid residues from about 1 to about 1115, inclusive of Figure 36 (SEQ ID NO.58), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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In yet another embodiment, the invention concerns agonists and arragonists of a native PRO1190 polypeptide. In a particular embodiment, the agonist or antagonist is an arti-PRO1190 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1190 polypeptide, by contacting the native PRO1190 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO1190 polypeptide, or an agonist or antagonist as bereinabove defined, in combination with a pharmaceutically acceptable carrier.

19. PRO177

A CDNA clane (DNA59817-1703) has been identified, having homology to nucleic acid encoding peptidane enzymes, that encodes a novel polypeptide, designated in the present application as 'PRO1772'.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO 1772 and verside.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (s) a DNA molecule encoding a PRO1772 polypeptide having the sequence of amino acid residues from about 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1772 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 93 or about 201 and about 1553, inclusive, of Figure 37 (SEQ ID NO:62). Preferably, hybridization occurs under stringent hybridization and weath conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encouling the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 202470 (DNA59817-1703) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 202470 (DNA59817-1703).

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In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 415

5 nucleotides and produced by bybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1772 polypeptide having the sequence of amino acid residues from 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO.63), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity (o), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1772 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 36 in the sequence of Figure 38 (SEQ ID NO:63). The transmembrane domain has been tentatively identified as extending from about amino acid position 313 to about amino acid position 331 in the PRO1772 amino acid sequence (Figure 38, SEQ ID NO:63).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more 20 preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1772 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,

25 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides the length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 37 (SEQ ID NO:62).

In another embodiment, the invention provides isolated PRO1772 polypeptide encoded by any of the isolated nucleic acid sequences bereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1772 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 37 to about 487 of Figure 38 (SEQ ID NO:63).

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In another aspect, the invention concerns an isolated PRO1772 polypeptide, comprising an amino acid sequence having at least about 80% sequence klemity, preferably at least about 80% sequence identity, more 35 preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO.63).

In a further aspect, the invention concerns an isolated PRO1772 polypeptide, comprising an amino acid

sequence scoring at least about 80% positives, preferably at least about 83% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63).

In yet another aspect, the invention concerns an isolated PRO1772 polypeptide, comprising the sequence of amino acid residues 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO:63), or a fragment thereof sufficient to provide a binding site for an anti-PRO1772 antibody. Preferably, the PRO1772 fragment retains a qualitative biological activity of a native PRO1772 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1772 polypeptide having the sequence of amino acid residues from about 1 or about 37 to about 487, inclusive of Figure 38 (SEQ ID NO.53), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and aniagonists of a native PRO1772 polypeptide. In a particular embodiment, the agonist or aniagonist is an anti-PRO1772 anithody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1772 polypeptide by contacting the native PRO1772 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1772 polypeptide, or an agontst or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

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20. PRO1248

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A cDNA clone (DNA60278-1530) has been identified, having homology to nucleic acid encoding PUT2, that encodes a novel polypeptide, designated in the present application as "PRO1248".

In one embodinem, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1248 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1248 polypeptide having the sequence of amino acid residues from about 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1248 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 122 or about 182 and about 670, inclusive, of Figure 39 (SEQ ID NO:67). Preferably, hybridization occurs under

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stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

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at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203170 (DNA60278-1530) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA emcoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203170 (DNA60278-1530).

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In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, proferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% requence identity to the sequence of amino acid residues 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1248 polypeptide having the sequence of amino acid residues from 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO.68), or (b) the complement of the DNA molecule of (a), and, 15 if the DNA molecule has at least about an 80 % sequence identity, preferrably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated meletic acid molecule comprising DNA encoding a PRO1248 polypeptide, with or without the N-terminal signal sequence and/or the initiating methicules, and 20 its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding multic acid molecule. The signal peptide has been tentarively identified as extending from about amino acid position 10 in the sequence of Figure 40 (SEQ ID NO:68). The transmembrane domain has been tentarively identified as extending from about amino acid position 90 to about amino acid position 112 in the PRO1248 amino acid sequence (Figure 40, SEQ ID NO:68).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1248 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleoides in length, preferably from about 20 to about 60 nucleoides in length, more preferably from about 20 to about 50 nucleoides in length and may be derived from the nucleoides acquence shown in Figure 39 (SEQ ID NO:67).

35 In another embodiment, the invention provides isolated PRO1248 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1248 polypeptide, which in

40 (SEQ ID NO:68). certain embodiments, includes an amino acid sequence comprising residues 1 or about 21 to about 183 of Figure

sequence of amino acid residues 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68). preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more In another aspect, the invention concerns an isolated PRO1248 polypeptide, comprising an amino acid

of residues 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68). sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence In a further aspect, the invention concerns an isolated PRO1248 polypeptide, comprising an amino acid

5 of amino acid residues 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID NO:68), or a fragment retains a qualitative biological activity of a native PRO1248 polypeptide thereof sufficient to provide a binding site for an anti-PRO1248 antibody. Preferably, the PRO1248 fragment In yet another aspect, the invention concerns an isolated PRO 1248 polypeptide, comprising the sequence

8 5 molecule under stringent conditions with (a) a DNA molecule euroding a PRO1248 polypeptide having the recovering the polypeptide from the cell culture. comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% NO:68), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell sequence of amino acid residues from about 1 or about 21 to about 183, inclusive of Figure 40 (SEQ ID In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1248 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1248

native PRO1248 polypeptide by contacting the native PRO1248 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

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or an agenist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO1248 polypeptide,

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novel polypeptide, designated in the present application as "PRO1316." A cDNA clone (DNA60608-1577) has been identified, having homology to Dickkopf that encodes a

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

ઝ preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1316 polypeptide having In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

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or (b) the complement of the DNA molecule of (a). the sequence of amino acid residues from 1 or about 26 to about 259, inclusive of Figure 42 (SEQ ID NO:70)

hybridization and wash conditions. about 987, inclusive, of Figure 41 (SEQ ID NO:69). Preferably, hybridization occurs under stringent polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 281 and in another aspect, the invention concerns an isolated aucleic acid molecule encoding a PRO1316

ö (DNA60608-1577), or (h) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic Deposit No. 203126 (DNA60608-1577). acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203126 about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

15 NO:70), or the complement of the DNA of (a). identity to the sequence of amino acid residues from about 26 to about 259, inclusive of Figure 42 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

8 25 Figure 41 (SEQ ID NO:69), or (b) the complement of the DNA malecule of (a). at least about 90% sequence identity, and most preferably at least about 95% sequence identity to: (a) a DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably of the DNA molecule of (a). Alternatively, an isolated nucleic acid molecule baving at least 15 nucleotides either from residues 1-454 or from residues 1095-3130 of the Figure 41 (SEQ ID NO:69), or (b) the complement molecule having a identity with a region spanning either from residues 1-454 or from residues 1095-3130 of the which hybridizes under stringent conditions with (a) a DNA molecule having a identity with a region spanning In a further aspect, the invention concern an isolated nucleic acid molecule having at least 15 nucleotides

30 1 to about amino acid position 25 in the sequence of Figure 42 (SEQ ID NO:70). An N-glycosylation site has its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding a PRO1316 polypopide, with or without the N-terminal signal sequence and/or the initiating methionine, and been identified at position 52 and a fungal Zn(2)-Cys(6) binuclear cluster has been identified at position 99. nucleic acid, molecule. The signal peptide has been tentatively identified as extending from amino acid position In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

amino acid sequence of residues 26 to about 259, inclusive of Figure 42 (SEQ ID NO:70), or (b) the complement preferably at least about 90% positives, most preferably at least about 95% positives when compared with the encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

ઝ of the DNA of (a).

In another embodiment, the invention provides isolated PRO1316 polypeptide encoded by any of the

isolated nucleic acid sequences herein above defined.

In a specific aspect, the invention provides isolated native sequence PRO1316 polypeptide, which in one rembodiment, includes an amino acid sequence comprising residues 26 to 259 of Figure 42 (SEQ ID NO:70).

In another aspect, the invention concerns an isolated PRO1316 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity in out preferably at least about 95% sequence identity to the sequence of amino acid residues 26 to about 259, inclusive of Figure 42 (SEQ ID NO:70).

In a further aspect, the invention concerns an isolated PRO1316 polypepitde, comprising an amino acid sequence acoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 26 to 259 of Figure 42 (SEQ ID NO:70).

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In yet another espect, the invention concerns an isolated PRO1316 polypeptide, comprising the sequence of amino acid residues 26 to about 259, inclusive of Figure 42 (SEQ ID NO.70), or a fragment thereof sufficient to provide a hinding site for m ami-PRO1316 antibody. Preferably, the PRO1316 fragment retains a qualitative biological activity of a native PRO1316 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1316 polypeptide having the sequence of amino acid residues from about 26 to about 259, inclusive of Figure 42 (SEQ ID NO:70), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence continuity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invantion concerns againsts and amagenists of the a native PRO1316 polypeptide. In a particular embodiment, the agonist or antagonist is an unit-PRO1316 ambody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1316 polypeptide, by contacting the native PRO1316 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO1316 polypeptide, or an agonist or antagonist as herein above defined, in combination with a pharmaceutically acceptable carrier.

22. PRO1197

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A cDNA clone (DNA60611-1524) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1197."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1197 polypeptide.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 80% sequence identity, most

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preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1197 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1197 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 383 and 5 about 1399, inclusive, of Figure 43 (SEQ ID NO:71). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203175 (DNA60611-1524), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203175 (DNA60611-1524).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypoptide having at least about 80% sequence identity, preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1197 polypeptide having the sequence of amino acid residues from about 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72), or (b) the complement 30 of the DNA of (a).

Another embodiment is directed to fragments of a PRO1197 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1197 polypeptide excoded by any of the isolated nucleic acid sequences hereinabove defined.

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In a specific aspect, the invention provides isolated native sequence PRO1197 polypeptide, which in one

embodiment, includes an amino acid sequence comprising residues 25 through 363 of Figure 44 (SEQ ID NO:72).

In another aspect, the invention concerns an isolated PRO1197 polypeptide, comprising an amino acid sequence having at least about 89% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity in the preferably at least about 95% sequence identity in the sequence of amino acid residues 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72).

In a further aspect, the invention concerns an isolated PRO1197 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, more preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 25 through 363 of Figure 44 (SEQ ID NO:72).

In yet another aspect, the invention concerns an isolated PRO1197 polypeptide, comprising the sequence of amino acid residues 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72), or a fragment thereof sufficient to provide a binding site for an anti-PRO1197 antibody. Preferably, the PRO1197 fragment retains a qualitative biological activity of a native PRO1197 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1197 polypeptide having the sequence of amino acid residues from about 25 to about 363, inclusive of Figure 44 (SEQ ID NO:72), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity in (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agenists and antagonists of a native PRO1197 polypeptide. In a particular embodiment, the agenist or antagonist is an anti-PRO1197 antibody.

25 23. PRO1293

A CDNA close (DNA60618-1557) has been identified, having homology to nucleic acid encoting an immunoglobulin heavy chain variable region protein that encodes a novel polypeptide, designated in the present application as "PRO1293".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1293 polypeptide.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1293 polypeptide having the sequence of amino acid residues from about 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an irolated nucleic acid molecule encoding a PRO1293 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 37

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or about 94 and about 1059, inclusive, of Figure 45 (SEQ ID NO:76). Preferably, hybridization occurs under tryberidization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 83% sequence identity, more preferably at least about 80% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203292 (DNA60618-1557) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

10 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
identity to the sequence of amino acid residues 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID

NO:77), or (b) the complement of the DNA of (a).

ATCC Deposit No. 203292 (DNA60618-1557).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100

15 nucleoxides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule emoding a PRO1293 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferrably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1293 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 19 in the sequence of Figure 46 (SEQ ID NO:77). The transmembrane domain has been tentatively identified as extending from about amino acid position 237 to about amino acid position 262 in the PRO1293 amino acid sequence (Figure 46, SEQ ID NO:77).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA cincoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more 30 preferably at least about 95% positives, more amino acid sequence of residues 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1293 polypeptide coding sequence that may find use as hybridization probes. Such nucleoic acid fragments are from about 20 to about 80 nucleotides in length, anore preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 45 (SEQ ID NO:76).

isolated nucleic acid sequences hereinabove identified. In another embodiment, the invention provides isolated PRO1293 polypeptide encoded by any of the

certain embodiments, includes an amino acid sequence comprising residues 1 or about 20 to about 341 of Figure In a specific aspect, the invention provides isolated native sequence PRO1293 polypeptide, which in

preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more sequence of amino acid residues 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77). In another aspect, the invention concerns an isolated PRO1293 polypeptide, comprising an amino acid

5 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least of residues 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77). about 90 % positives, most preferably at least about 95 % positives when compared with the amino acid sequence In a further aspect, the invention concerns an isolated PRO1293 polypeptide, comprising an amino acid

thereof sufficient to provide a binding site for an anti-PRO1293 antibody. Preferably, the PRO1293 fragment retains a qualitative biological activity of a native PRO1293 polypeptide. of amino acid residues 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID NO:77), or a fragment In yet another aspect, the invention concerns an isolated PRO1293 polypeptide, comprising the sequence

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NO:77), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% recovering the polypeptide from the cell culture. sequence of amino acid residues from about 1 or about 20 to about 341, inclusive of Figure 46 (SEQ ID molecule under stringent conditions with (a) a DNA molecule encoding a PRO1293 polypeptide having the sequence identity, most preferably at least about a 95% requence identity to (a) or (b), (ii) culturing a host cell In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

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23 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1293 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1293

monitoring a biological activity mediated by said polypeptide native PRO1293 polypeptide by contacting the native PRO1293 polypeptide with a candidate molecule and In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier. in a still further embodiment, the invention concerns a composition comprising a PRO1293 polypeptide.

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polypeptide designated in the present application as "PRO1380". A cDNA clone (DNA60740-1615) has been identified that encodes a novel multi-span transmembrane

a PRO1380 polypeptide. In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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the complement of the DNA molecule of (a). the sequence of amino acid residues from about 1 to about 470, inclusive of Figure 48 (SEQ ID NO:79), or (b) preferably at least about 95 % sequence identity to (a) a DNA molecule encoding a PRO1380 polypeptide baving preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity.

hybridization and wash conditions, about 1460, inclusive, of Figure 47 (SEQ ID NO:78). Preferably, hybridization occurs under stringent polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 36 and In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1380

15 5 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least Deposit No. 203456 (DNA60740-1615). (DNA60740-1615), or (h) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203456 about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

NO:79), or the complement of the DNA of (a). identity to the sequence of amino acid residues from about 1 to about 470, inclusive of Figure 48 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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ß of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably amino acid residues from about 1 to about 470, inclusive of Figure 48 (SEQ ID NO:79), or (b) the complement under stringem conditions with (a) a DNA molecule encoding a PRO1380 polypeptide having the sequence of nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

30 a PRO1380 polypeptide, and its soluble variants (i.e. one or more transmembrane domains deleted or inactivated), or is complementary to such encoding nucleic acid molecule. Transmembrane domains have been 305-330, and 448-472 in the PRO1380 amino acid sequence (Figure 48, SEQ ID NO:79). tentatively identified at about the following amino acid positions: 50-74, 105-127, 135-153, 163-183, 228-252. In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

ដ preferably at least about 90% positives, most preferably at least about 95% positives when compared with the of the DNA of (a). amino acid sequence of residues 1 to about 470, inclusive of Figure 48 (SEQ ID NO:79), or (b) the complement encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

Another embodiment is directed to fragments of a PRO1380 polypepside coding sequence that may find use as hybridization probes. Such mucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 80 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length,

In another embodiment, the invention provides isolated PRO 1380 polypeptide encoded by any of the S isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1380 polypepside, which in one embodiment, includes an amino acid sequence comprising residues 1 to 470 of Figure 48 (SEQ ID NO:79).

In another supect, the invention concerns an isolated PRO 1380 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity in the preferably at least about 90% sequence identity to the sequence of amino acid residues 1 to about 470, inclusive of Figure 48 (SEQ ID NO:79).

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In a further aspect, the invention concerns an isolated PRO1380 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 470 of Figure 48 (SEQ ID NO:79).

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In yet another expect, the invention concerns an isolated PRO1380 polypeptide, comprising the sequence of amino acid residues 1 to about 470, inclusive of Figure 48 (SEQ ID NO:79), or a fragment thereof sufficient to provide a binding site for an ami-PRO1380 antibody. Preferably, the PRO1380 fragment retains a qualitative biological activity of a native PRO1380 polypeptide.

20 In a still further aspect, the invention provides a polypeptide produced by (i) hybridzing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1380 polypeptide having the sequence of amino acid residues from about 1 to about 470, inclusive of Figure 48 (SEQ ID NO:79), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a bost cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

5. PRO1265

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A cDNA clone (DNA60764-1533) has been identified that encodes a novel polypeptide having bomology to the Fig1 polypeptide and designated in the present application as "PRO1265."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1265 polypeptide.

In one aspect, the isolated macleic acid comprises DNA having at least about 80% sequence identity,

35 preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most

preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1265 polypeptide having

the sequence of amino acid residues from 1 or about about 22 to about 567, inclusive of Figure 50 (SEQ ID

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NO:84), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1265 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 142 and about 1779, inclusive, of Figure 49 (SEQ ID NO:83). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns on isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203452 (DNA60764-1533), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic DNA60764-1533) and DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC

In a still further aspect, the invertion concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity to the sequence of antino acid residues from about 22 to about 567 inclusive of Flavors 60 (SEO III).

Deposit No. 203452 (DNA60764-1533).

15 identity to the sequence of amino acid residues from about 22 to about 567, inclusive of Figure 50 (SEQ ID NO:84), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1265 polypeptide having the sequence of amino acid residues from about 22 to about 567, inclusive of Figure 50 (SEQ ID NO:84), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity to (a) or (b), kolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding 25 a PRO1255 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 21 in the sequence of Figure 50 (SEQ ID NO:84).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA 30 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 22 to about 567, inclusive of Figure 50 (SEQ ID NO:84), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1265 polypeptide coding sequence that may find

55 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
preferably from about 20 to about 60 nucleotides in tength, more preferably from about 20 to about 50

nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1265 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1265 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or about 22 to 567 of Figure 50 (SEQ ID NO:54).

In another aspect, the invention concerns an isolated PRO1265 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 22 to about 567, inclusive of Figure 50 (SEQ ID NO:84).

In a further aspect, the invention concerns an isolated PRO1265 polypeptide, comprising an amino acid

10 requence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least
about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence
of residues 22 to 567 of Figure 50 (SEQ ID NO:84).

In yet another aspect, the invention concerns an isolated PRO1265 polypepilde, comprising the sequence of amino acid residues 22 to about 567, inclusive of Figure 50 (SEQ ID NO:84), or a fragment thereof sufficient to provide a binding site for an ami-PRO1265 antibody. Preferably, the PRO1265 fragment retains a qualitative biological activity of a native PRO1265 polypepilde.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1265 polypeptide having the sequence of amino acid residues from about 22 to about 567, inclusive of Figure 50 (SEQ ID NO:84), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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26. PRO1250

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A cDNA clone (DNA60775-1532) has been identified, having homology to nucleic acid encoding long chain farry acid CoA ligase that encodes a novel polypeptide, designated in the present application as "PRO1250".

In one embodimens, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1250 polypeptide.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1250 polypeptide having the sequence of amino acid residues from about 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1250

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polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 74 and about 2290, inclusive, of Figure 51 (SEQ ID NO:85). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203173 (DNA60775-1532) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203173 (DNA60775-1532).

In still a further aspect, the invention concerns an isolated medeic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 medeotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1250 polypeptide having the sequence of amino acid residues from 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85 % sequence identity, most preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated modelic acid molecule comprising DNA exceding a PRO1250 polypeptide, with or without the initiating methlonine, and its soluble, i.e., transmembrane domain deleted or itaartivated variants, or is complementary to such encoding nucleic acid molecule. The type II 25 transmembrane domain has been tentatively identified as extending from shout amino acid position 61 to about amino acid position 80 in the PRO1250 amino acid sequence (Figure 52, SEQ ID NO:86).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 80% positives, more preferably at least about 80% positives, more preferably at least about 90% positives, more preferably at least about 90% positives, more preferably at least about 90% positives when compared with the

30 amino acid sequence of residues I to about 739, inclusive of Figure 52 (SEQ ID NO.86), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1250 polypeptide coding sequence that may find use us bybridization probes. Such mucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 51 (SEQ ID NO:85).

In another embodiment, the invention provides isolated PRO1250 polypeptide encoded by any of the

isolated nucleic acid sequences hereinabove identified.

certain embodiments, includes an amino acid sequence comprising residues 1 to about 739 of Figure 52 (SEQ In a specific aspect, the invention provides isolated native sequence PRO1250 polypeptide, which in

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues I to about 739, inclusive of Figure 52 (SEQ ID NO:86). In another aspect, the invention concerns an isolated PRO1250 polypeptide, comprising an amino acid

about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86). sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated PRO1250 polypeptide, comprising an amino acid

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biological activity of a native PRO1250 polypeptide. of amino acid residues 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86), or a fragment thereof sufficient to provide a binding site for an anti-PRO1250 antibody. Preferably, the PRO1250 fragment retains a qualitative In yet another aspect, the invention concerns an isolated PRO 1250 polypeptide, comprising the sequence

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polypeptide from the cell culture. the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising sequence of amino acid residues from about 1 to about 739, inclusive of Figure 52 (SEQ ID NO:86), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence molecule under stringent conditions with (a) a DNA molecule encoding a PRO1250 polypeptide having the In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

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polypeptide. In a particular embodiment, the agonist or aniagonist is an anti-PRO1250 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1250

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native PRO1250 polypeptide by contacting the native PRO1250 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide. In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a

30 or an agonist or untagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invertion concerns a composition comprising a PRO1250 polypeptide,

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N-acetylghucosaminyltransferase that encodes a novel polypeptide, designated in the present application as A cDNA clone (DNA61185-1646) has been identified, having homology to nucleic acid encoding an

a PRO1475 polypeptide. In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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the complement of the DNA molecute of (a). the sequence of amino acid residues from about 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88), or (b) preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1475 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity.

hybridization and wash conditions. and about 2109, inclusive, of Figure 53 (SEQ ID NO:87). Preferably, hybridization occurs under stringent polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 130 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1475

15 5 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least ATCC Deposit No. 203464 (DNA61185-1646). nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in (DNA61185-1646) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the encoting the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203464 about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

the complement of the DNA of (a). encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity to the sequence of amino acid residues 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88), or (b) dentity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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23 or (b), isolating the test DNA molecule. preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) molecule has at least about an 80% sequence identity, prefereably at least about an 85% sequence identity, more molecule encoding a PRO1475 polypeptide having the sequence of amino acid residues from 1 to about 660, nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA inclusive of Figure 54 (SEQ ID NO:88), or (b) the complement of the DNA molecule of (a), and, if the DNA In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 180

30 deletted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane position 55 in the PRO1475 amino acid sequence (Figure 54, SEQ ID NO:88). domain has been tentatively identified as extending from about amino acid position 38 to about amino acid a PRO1475 polypeptide, with or without the initiating methionine, and its soluble, i.e., transmembrane domain In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

35 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the of the DNA of (a). amino acid sequence of residues 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88), or (b) the comptement encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

Another embodiment is directed to fragments of a PRO1475 polypepside coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and must preferably from about 20 to about 40 nucleotides in length and must preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 53 (SEQ ID NO:87).

In another embodiment, the invention provides isolated PRO1475 polypeptide encoded by any of the isolated mucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1475 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 660 of Figure 54 (SEQ ID NO:85).

10 In another aspect, the invention concerts an isolated PRO1475 polypeptide, comprising an amino axid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity in the preferably at least about 90% sequence identity to the sequence of amino axid residues 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88).

In a further aspect, the invention concerns an isolated PRO 1475 polypepide. comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88).

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In yet another aspect, the invention concerns an isolated PRO1475 polypeptide, comprising the sequence of amino acid residues 1 to about 660, inclusive of Figure 54 (SEQ ID NO:88), or a fragment thereof sufficient to provide a binding site for an anti-PRO1475 antibody. Preferably, the PRO1475 fragment retains a qualitative biological activity of a native PRO1475 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1475 polypeptide having the sequence of amino acid residues from about 1 to about 660, inclusive of Figure 54 (SSQ ID NO:88), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under coaditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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30 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1475 polypepide. In a particular embodiment, the agonist or amagonist is an ami-PRO1475 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1475 polypeptide by contacting the native PRO1475 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

35 In a still further embodiment, the invention concerns a composition comprising a PRO 1475 polypeptide, or an agonist or amagonist as bereinabove defined, in combination with a pharmaceutically acceptable carrier

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28. PRO1377

A cDNA clone (DNA61608-1606) has been identified that encodes a novel multi-span transmembrane polypeptide designated in the present application as "PRO1377."

In one embodiment, the invention provides an isolated nucleic usid molecule comprising DNA encoding PRO1377 polypoptide.

In one aspert, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1377 polypeptide having the sequence of amino acid restitues from 1 or about 19 to about 307, inclusive of Figure 56 (SEQ ID NO:95), or (b) the complement of the DNA molecule of (a).

10 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1377 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 203 and about 1069, inclusive, of Figure 55 (SEQ ID NO:94). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

15 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least
about 90% sequence identity, most preferably at least about 95% acquence identity to (a) a DNA molecule
emoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203239

(DNA61608-1606), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic
acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC

20 Deposit No. 203239 (DNA61608-1606).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA excooling a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 307, inclusive of Figure 56 (SEQ ID NO:95), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1377 polypeptide having the sequence of amino acid residues from about 19 to about 307, inclusive of Figure 56 (SEQ ID NO:95), or (b) the complement

30 of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1377 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and 35 one or more of its transmembrane domains deleted or inactivated, or is complementary to such excoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 18 in the sequence of Figure 56 (SEQ ID NO:95). Transmembrane domain

has been remainely identified as extending from about amino acid positions 37-56, 106-122, 211-20, 240-260, and 288-304 in the PRO1377 amino acid sequence (Figure 56, SEQ ID NO:95).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 90% positives when compared with the amino acid sequence of residues 19 to about 90%, inclusive of Figure 56 (SEQ ID NO:95), or (b) the complement of the DNA of (a)

Another embodiment is directed to fragments of a PRO1377 polypeptide coding sequence that may find use as hybridization probest. Such mucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1377 polypopoids encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1377 polypopide, which in one embodiment, includes an amino acid sequence comprising residues 19 to 307 of Figure 56 (SEQ ID NO:95).

In another sepect, the invention concerns an isolated PRO1377 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 307, inclusive of Figure 56 (SEQ ID NO:95).

In a further aspect, the invention concerns an isolated PRO1377 polypeptide, comprising an amino acid

20 exquence according at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to 307 of Figure 56 (SEQ ID NO:95).

In yet another aspect, the invention concerns an isolated PRO1377 polypeptide, comprising the sequence of amino acid residues 19 to about 307, inclusive of Figure 56 (SEQ ID NO.95), or a fragment thereof sufficient to provide a binding site for an anti-PRO1377 antibody. Preferably, the PRO1377 fragment retains a qualitative biological activity of a native PRO1377 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a rest DNA molecule under stringent conditions with (a) a DNA molecule emoding a PRO1377 polypeptide having the sequence of amino acid residues from about 19 to about 307, inclusive of Figure 56 (SEQ ID NO:55), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 80% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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PRO1326

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A cDNA clone (DNA62808-1382) has been identified that encodes a novel secreted polypeptide

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designated in the present application as "PRO1326."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1326 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1326 polypeptide having the sequence of amino acid residues from 1 or about 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100), or (b) the complement of the DNA molecule of (a).

In mother aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1326 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 199 and about 1314, inclusive, of Figure 57 (SEQ ID NO.99). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity. most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203388 (DNA62808-1582), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203388 (DNA62808-1582).

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

20 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
identity to the sequence of amino acid residues from about 30 to about 401, inclusive of Figure 58 (SEQ ID

NO:100), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1326 polypeptide having the sequence of amino acid residues from about 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about a 80% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated metric acid molecule comprising DNA encoding a PRO1326 polypepside, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tensuively identified as extending from anino acid position 1 through about amino acid position 29 in the sequence of Figure 58 (SEQ ID NO:100).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DN/ encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, mon

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preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1326 polypepide coding sequence that may find use at hybridization probes. Such mulcie acid fragments are from about 20 to about 80 nuclenities in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

in another embodiment, the invention provides isolated PRO1325 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific sepect, the invention provides isolated taxive sequence PRO1326 polypeptide, which in one 10 cmbodiment, includes an amino acid sequence comprising residues 30 to 401 of Figure 58 (SEQ ID NO:100).

In another aspect, the invention concerns an isolated PRO1326 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100).

In a further aspect, the invention concerns an isolated PRO 1326 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 30 to 401 of Figure 58 (SEQ ID NO: 100).

In yet another aspect, the invention concerns an isolated PRO1326 polypeptide, comprising the sequence of amino acid residues 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100), or a fragment thereof sufficient to provide a binding site for an ami-PRO1326 amihody. Preferably, the PRO1326 fragment retains a qualitative biological activity of a native PRO1326 polypeptide.

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In a still further espect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1326 polypeptide having the sequence of amino acid residues from about 30 to about 401, inclusive of Figure 58 (SEQ ID NO:100), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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30. FRO124

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A cDNA clone (DNA62809-1531) has been identified that encodes a novel transmembrane polypeptide, designated in the present application as "PRO1249".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO 1249 polypeptide.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

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preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1249 polypeptide having the sequence of amino acid residues from about 1 or about 17 to about 1089, Inclusive of Figure 60 (SEQ ID NO:102), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule emouling a PRO1249 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 3 or about 51 and about 3269, inclusive, of Figure 59 (SEQ ID NO:101). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule exceeding the same mature polypeptide exceeded by the human protein cDNA in ATCC Deposit No. 203237 (DNA62809-1531) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA exceeding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203237 (DNA62809-1531).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, proferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102), or (b) the complement of the DNA of (a).

20 In a further aspect, the invention concerns an isolated nucleic acid molecule baving at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1249 polypeptide having the sequence of amino acid residues from 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85 % sequence identity, most preferably at least about a 95 % sequence identity, on the preferably at least about a 95 % sequence identity, on the preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1249 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionize, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or it complementary to such encoding mucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 16 in the sequence of Figure 60 (SEQ ID NO:102). The transmembrane domains have been tentatively identified as extending from about amino acid position 317 to about amino acid position 341, from about amino acid position 451 to about amino acid position 470, from about amino acid position 481 to about amino acid position 500, from about amino acid position 510 to about amino acid position 535, from about amino acid position 537, from about amino acid position 538 to about amino acid position 555, from about amino acid position 500, from about amino acid position 500 acid and from about amino acid position 500 acid acid acid sequence

(Figure 60, SEQ ID NO:102).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA cucoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1249 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 59 (SEQ ID NO: 101).

In another embodiment, the invention provides isolated PRO1249 polypeptide encoded by any of the isolated multic acid sequences hereinabove identified.

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In a specific aspect, the invention provides tonlated native sequence PRO1249 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 17 to about 1089 of Figure 60 (SEQ ID NO:102).

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In another espect, the invention concerns an isolated PRO1249 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102).

In a further expect, the invention concerns an isolated PRO1249 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, proferably at least about 80% positives, more preferably at least about 90% positives, more preferably at least about 90% positives when computed with the amino acid sequence of residues 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO: 102).

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In yet another aspect, the invention concerns an isolated PRO1249 polypeptide, comprising the sequence of amino acid residues 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102), or a fragment thereof sufficient to provide a binding site for an anti-PRO1249 antibody. Preferably, the PRO1249 fragment retains a qualitative biological activity of a native PRO1249 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1249 polypeptide having the sequence of amino acid residues from about 1 or about 17 to about 1089, inclusive of Figure 60 (SEQ ID NO:102), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) 35 recovering the polypeptide from the cell culture.

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A cDNA clone (DNA62815-1576) has been identified, having homology to nucleic acid encoding cytokine receptor family-4 proteins that encodes a novel polypeptide, designated in the present application as "PRO1315".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding . PRO1315 pulypeptide.

In one aspect, the isolated nuclcic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1315 polypeinide having the sequence of amino acid residues from about 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO:104), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid moleculo encoding a PRO1315 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 121 or about 205 and about 1446, inclusive, of Figure 61 (SEQ ID NO:103). Preferably, hybridization occurs under stringent hybridization and wash conditions.

Is the a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203247 (DNA62815-1576) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA eacoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203247 (DNA62815-1576).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence.

25 identity to the sequence of amino acid residues 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO:104), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 500 nucleosides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1315 polypeptide having the sequence of amino acid residues from 1 or about 29 to 30 about 442, inclusive of Figure 62 (SEQ ID NO:104), or (b) the complement of the DNA molecule of (a), and

about 442, inclusive of Figure 62 (SEQ ID NO:104), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

in a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding
35 a PRO1315 polypeptide, with or without the N-terminal signal sequence and/or the initiating methonine, and
its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding
nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid

position I to about amino acid position 28 in the sequence of Figure 62 (SEQ ID NO:104). The transmembrane domain has been tensatively identified as extending from about amino acid position 140 to about amino acid position 163 in the PRO1315 amino acid sequence (Figure 62, SEQ ID NO:104).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, proferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO:104), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO/1315 polypoptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 61 (SEQ ID NO:103).

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In another embodiment, the invention provides isolated PRO1315 polypeptide encoded by any of the isolated queletic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1315 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 29 to about 442 of Figure 62 (SEQ ID NO:104).

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In another aspect, the invention concerns an isolated PRO1315 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to the sequence of amino acid residues 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO:104).

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In a further aspect, the invention concerns an isolated PRO 1315 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO: 104).

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In yet another aspect, the invention concerns an isolated PRO1315 polypeptide, comprising the sequence of amino acid residues 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO:104), or a fragment thereof sufficient to provide a binding site for an anti-PRO1315 antibody. Preferably, the PRO1315 fragment retains a qualitative biological activity of a native PRO1315 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1315 polypeptide having the sequence of amino acid residues from about 1 or about 29 to about 442, inclusive of Figure 62 (SEQ ID NO:104), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about as 80% sequence identity, preferably at least about as 80% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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In yet another embodiment, the invention concerns agonists and amagonists of a native PRO1315 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1315 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a native PRO1315 polypeptide by contacting the native PRO1315 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1315 polypeptide or an agonist or antagonist as hereinabove defined, in combination with a pharmacentically acceptable carrier

32. PRO1599

A cDNA clone (DNA62845-1694) has been identified that encodes a novel polypeptide having homology

10 to Granzyme M and designated in the present application as "PRO1599."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1599 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most 15 preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1599 polypeptide having the sequence of amino acid residues from 1 or about 31 to about 283, inclusive of Figure 64 (SEQ ID NO:111), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated mackete acid molecule encoding a PRO1599 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 159 and 20 about 917, inclusive, of Figure 63 (SEQ ID NO:110). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an stolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule 25 encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203361 (DNA62845-1684), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203361 (DNA62845-1684).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

30 encoding a polypepside having at least about 80% sequence identity, preferably at least about 85% sequence
identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
identity to the sequence of amino acid residues from about 31 to about 283, inclusive of Figure 64 (SEQ ID

NO:111), or the complement of the DNA of (a).

In a further expect, the invention concerns an isolated nucleic acid molecule having at least about 50

35 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1599 polypeptide having the sequence of amino acid residues from about 31 to about 283, inclusive of Figure 64 (SEQ ID NO:111), or (b) the

complement of the DNA molecule of (a), and, if the DNA molecule has at least about in 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity in (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1599 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 30 in the sequence of Figure 64 (SEQ ID NO:111).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to about 283, inclusive of Figure 64 (SEQ ID NO:111), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1599 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1599 polypeptide encoded by any of the isolated mucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1599 polypeptide, which in one

20 embodiment, includes an amino acid sequence comprising residues 31 to 283 of Figure 64 (SEQ ID NO:111). In another aspect, the invention concerns an isolated PRO1599 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 31 to about 283, inclusive of Figure 64 (SEQ ID NO:111).

25 in a further aspect, the invention concerns an isolated PRO1599 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to 283 of Figure 64 (SEQ ID NO:111).

In yet another aspect, the inversion concerns an isolated PRO1599 polypeptide, comprising the sequence 30 of amino acid residues 31 to about 283, inclusive of Figure 64 (SEQ ID NO:111), or a fragment thereof sufficient to provide a binding site for an anti-PRO1599 antibody. Preferably, the PRO1599 fragment retains a qualitative biological activity of a native PRO1599 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1599 polypeptide having the sequence of antino acid residues from about 31 to about 283, inclusive of Figure 64 (SEQ ID NO:1111), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 85% sequence

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identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a bost cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agunists and antagonists of a native PRO1599 polypeptide. In a particular embodiment, the agentst or antagonist is an anti-PRO1599 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a native PRO1599 polypeptide, by contacting the native PRO1599 polypeptide with a candidate molecule and monatoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1599 polyecptide, or an agonist or amagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

33. PRO143

A cDNA clone (DNA64842-1632) has been identified that encodes a novel polypeptide having homology to reductase proteins, designated in the present application as *PRO1430.*

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

15 a PRO1430 polypeptide.

In one aspect, the isolated mucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1430 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid malecule encoding a PRO1430 polypeptide comprising DNA hybridizing to the complement of the modele acid between about residues 33 and about 1074, inclusive, of Figure 65 (SEQ ID NO:115). Preferably, hybridization occurs under stringent bybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203278 (DNA64842-1632), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203278 (DNA64842-1632).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. DNA molecule of (a), and, if the DNA mulecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least residues from about 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116), or (b) the complement of the conditions with (a) a DNA molecule encoding a PRO1430 polypeptide having the sequence of amino acid nucleotides, and preferably at least about 100 and produced by hybridizing a test DNA molecule under stringent

nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position I through about amino acid position 17 in the sequence of Figure 66 (SEQ ID NO:116). a PRO1430 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding v

complement of the DNA of (a). preferably at least about 90% positives, most preferably at least about 95% positives when compared with the encoding a polypeptide scoring at least about 80% pusitives, preferably at least about 85% positives, more amino acid sequence of residues 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116), or (b) the In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

ᅜ preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length. Another embodiment is directed to fragments of a PRO1430 polypeptide coding sequence that may find

isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated PRO1430 polypeptide encoded by any of the

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embodiment, includes an amino acid sequence comprising residues 18 to 331 of Figure 66 (SEQ ID NO:116). In a specific aspect, the invention provides isolated native sequence PRO 1430 polypeptide, which in one

preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more sequence of amino acid residues 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116). In another aspect, the invention concerns an isolated PRO1430 polypeptide, comprising an amino acid

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of residues 18 to 331 of Figure 66 (SEQ ID NO:116) sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence In a further aspect, the invention concerns an isolated PRO1430 polypeptide, comprising an amino acid

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a qualitative biological activity of a native PRO1430 polypeptide. sufficient to provide a binding site for an anti-PRO1430 antibody. Preferably, the PRO1430 fragment retains of amino acid residues 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116), or a fragment thereof In yet another aspect, the invention concerns an isolated PRO1430 polypeptide, comprising the sequence

ä molecule under stringent conditions with (a) a DNA molecule encoding a PRO1430 polypoptide having the sequence of amino acid residues from about 18 to about 331, inclusive of Figure 66 (SEQ ID NO:116), or (b) In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

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identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising polypeptide from the cell culture. the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1430 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1430

monituring a biological activity mediated by said polypeptide native PRO1430 polypeptide, by contacting the native PRO1430 polypeptide with a candidate molecule and In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a

10 or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO 1430 polypeptide

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15 identity with P4HA and designated in the present application as "PRO1374." A cDNA clone (DNA64849-1604) has been identified that encodes a novel polypeptide having sequence

a PRO1374 polypeptide. In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

20 preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1374 polypeptide having or (b) the complement of the DNA molecute of (a). the sequence of arrino acid residues from 1 or about 20 to about 344, inclusive of Figure 68 (SEQ ID NO:118) preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity

25 hybridization and wash conditions. about 1652, inclusive, of Figure 67 (SEQ ID NO:117). Preferably, hybridization occurs under stringent polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 78 and In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO137.

(DNA64849-1604), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203468 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at leas about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

30 Deposit No. 203468 (DNA64849-1604). acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCO

35 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity to the sequence of amino acid residues from about 20 to about 544, inclusive of Figure 68 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DN/

NO:118), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleonides, and preferably at least about 100 nucleonides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1374 polypeptide having the sequence of amino acid residues from about 20 to about 544, inclusive of Figure 68 (SEQ ID NO:118), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 to about 544, inclusive of Figure 68 (SEQ ID NO:118), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1374 polypeptide coding sequence that may find use as bybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1374 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

ln a specific aspect, the invention provides isolated native acquence PRO1374 polypopide, which in one
20 embodiment, includes an amino acid sequence comprising residues 20 through 544 of Figure 68 (SEQ ID
NO:118).

In another aspect, the invention concerns an isolated PRO1374 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 20 to about 544, inclusive of Figure 68 (SEQ ID NO:118).

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In a further aspect, the invention concerns an isolated PRO1374 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 20 through 544 of Figure 68 (SEQ ID NO:118).

In yet another aspect, the invention concerns an isolated PRO1374 polypoptide, comprising the sequence of amino acid residues 20 to about 544, inclusive of Figure 68 (SEQ ID NO:118), or a fragment thereof sufficient to provide a binding site for an anti-PRO1374 antibody. Preferably, the PRO1374 fragment retains a qualitative biological activity of a native PRO1374 polypoptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA 35 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1374 polypeptide having the sequence of amino acid residues from about 20 to about 544, inclusive of Figure 68 (SEQ ID NO:118), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence

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identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the collection the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1374 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1374 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a mative PRO1374 polypeptide, by contacting the native PRO1374 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO 1374 polypeptide

10 or an agonist or antagonist as bereinabove defined, in combination with a pharmaceutically acceptable carrier

35. PRO131

A cDNA clone (DNA64863-1573) has been identified that encodes a novel terraspan polypeptide designated in the present application as "PRO1311".

15 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO 1311 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1311 polypepidde having 20 the sequence of amino acid residues from 1 or about 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123).

or (b) the complement of the DNA molecule of (a),

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1311 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 327 and about 1076, inclusive, of Figure 69 (SEQ ID NO:122). Preferably, hybridization occurs under stringent 25 hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity on (a) a DNA molecule about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203251

30 (DNA64863-1573), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCO Deposit No. 203251 (DNA64863-1573).

in a still further aspect, the invernion concerns an isolated nucleic acid molecule comprising (a) DNA encoting a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123), or the complement of the DNA of (a).

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preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most complement of the UNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. amino acid residues from about 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123), or (b) the under stringent conditions with (a) a DNA molecule encoding a PRO1311 polypeptide having the sequence of nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position in the PRO1311 amino acid sequence (Figure 70, SEQ ID NO:123). domains has been tentatively identified as extending from about amino acid 22-42, 57-85, 94-116, and 230-257 its soluble, i.e. transmembrane domains deleted or inactivated variants, or is complementary to such encoding a PRO1311 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and I through about amino acid position 44 in the sequence of Figure 70 (SEQ ID NO:123). Four transmembrane In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more amino acid sequence of residues 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123), or (b) the preferably at least about 90% positives, most preferably at least about 95% positives when compared with the complement of the DNA of (a). In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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20 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, nuclectides in length, and most preferably from about 20 to about 40 nucleotides in length. preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 Another embodiment is directed to fragments of a PRO1311 polypeptide coding sequence that may find

isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated PRO1311 polypeptide encoded by any of the

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sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more embodiment, includes an amino acid sequence comprising residues 45 to 294 of Figure 70 (SEQ ID NO:123) In another aspect, the invention concerns an isolated PRO1311 polypeptide, comprising an amino acid In a specific aspect, the invention provides isolated native sequence PRO1311 polypeptide, which in one

of residues 45 to 294 of Figure 70 (SEQ ID NO: 123). about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence ecquence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated PRO1311 polypeptide, comprising an amino acid 30

sequence of amino acid residues 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123).

preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the

ĸ of amino acid residues 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123), or a fragment thereof sufficient to provide a binding site for an anti-PRO1311 antibody. Preferably, the PRO1311 fragment retains In yel another aspect, the invention concerns an isolated PRO1311 polypeptide, comprising the sequence

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a qualitative biological activity of a native PRO1311 polypeptide

identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence the test DNA molecule under couditions suitable for expression of the polypeptide, and (iii) recovering the identity, most preferably at least about a 95 % sequence identity to (a) or (b), (ii) culturing a host cell comprising polypeptide from the cell culture. sequence of amino acid residues from about 45 to about 294, inclusive of Figure 70 (SEQ ID NO:123), or (b) molecule under stringent conditions with (a) a DNA molecule encoding a PRO1311 polypeptide having the In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DN.

33, PRO1357

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as "PRO1357". von Ebner minor salivary gland protein that encodes a novel polypeptide, designated in the present application A cDNA clone (DNA64881-1602) has been identified, having homology to nucleic acid encoding the

a PRO1357 polypeptide. In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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NO:128), or (b) the complement of the DNA molecule of (a). preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1357 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most the sequence of amino acid residues from about 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity

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stringent hybridization and wash conditions. or about 137 and about 1525, inclusive, of Figure 71 (SEQ ID NO:127). Preferably, hybridization occurs under polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 74 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1357

30 25 nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least (DNA64881-1602) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the ATCC Deposit No. 203240 (DNA64881-1602). encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203240 about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

35 identity to the sequence of amino acid residues 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

NO:128), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 40

nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1357 polypeptide having the sequence of amino acid residues from 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, proferrably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1357 polypepitde, with or without the N-terminal signal sequence and/or the initiating methionitie, or is complementary to such encoding nucleic acid molecule. The signal poptide has been tentatively identified as extending from about amino acid position I to about amino acid position 21 in the sequence of Figure 72 (SEQ ID NO:128).

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In mother aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1357 polypeptide coding scquence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 71 (SEQ ID NO:127).

In another embodiment, the invention provides isolated PRO1357 polypeptide encoded by any of the isolated mucleic acid sequences hereinabove identified.

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In a specific aspect, the invention provides isolated native sequence PRO1357 polypeptide, which in certain embodiments, includes an umino acid sequence comprising residues I or about 22 to about 484 of Figure 72 (SEQ ID NO:128).

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In another aspect, the invention concerns an isolated PRO1357 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128).

30 In a further aspect, the invention concerns an isolated PRO1137 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128).

In yet another aspect, the invention concerns an isolated PRO1357 polypeptide, comprising the sequence of amino acid residues 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128), or a fragment thereof sufficient to provide a binding site for an anti-PRO1357 antibody. Preferably, the PRO1357 fragment retains a qualitative biological activity of a native PRO1357 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1357 polypeptide having the sequence of amino acid residues from about 1 or about 22 to about 484, inclusive of Figure 72 (SEQ ID NO:128), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yot another embodiment, the invention concerns agonists and antagonists of a native PRO1357 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1357 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1357 polypeptide by contacting the native PRO1357 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO1357 polypepide or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

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A cDNA clone (DNA64883-1326) has been identified that encodes a novel polypeptidehaving homology to Implantation-Associated Protein and designated in the present application as "PRO1244."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding 20 a PRO1244 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1244 polypeptide having the sequence of amino acid residues from 1 or about 30 to about 335, inclusive of Figure 74 (SEQ ID NO:130), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1244 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 96 and about 1013, inclusive, of Figure 73 (SEQ ID NO:129). Preferably, bybridization accurs under stringent bybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203253 (DNA64883-1526), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the medeic 35 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203253 (DNA64881-1526).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DN/

encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 30 to about 315, inclusive of Figure 74 (SEQ ID NO:130), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1244 polypeptide having the sequence of amino acid residues from about 30 to about 335, inclusive of Figure 74 (SEQ ID NO:130), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated metric acid molecule comprising DNA encoding a PRO1244 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionize, and its soluble, i.e. transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 29 in the sequence of Figure 74 (SEQ ID NO:130). The transmembrane domains have been tentatively identified in the PRO1244 amino acid sequence at about the following amino acid regions: 183-205, 217-137, 271-287, and 301-321.

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more 200 preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 30 to about 335, inclusive of Figure 74 (SEQ ID NO:130), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1244 polypeptide coding sequence that may find use as hybridization probes. Such aucleic acid fragments are from about 20 to about 80 nucleotides in length, 25 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1244 polypeptide encoded by any of the isolated macleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1244 polypeptide, which in one 30 embodiment, includes an amino acid sequence comprising residues 30 to 335 of Figure 74 (SEQ ID NO.130). In another aspect, the invention concerns an isolated PRO1244 polypeptide, comprising an amino acid sequence having at least about 85% sequence identity, preferably at least about 85% sequence identity, more

35 In a further aspect, the invention concerns an isolated PRO1244 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 80% positives, more preferably at least about 90% positives, more preferably at least about 90% positives, more preferably at least about 90% positives when compared with the amino acid sequence

sequence of amino acid residues 30 to about 335, inclusive of Figure 74 (SEQ ID NO:130),

preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the

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of residues 30 to 335 of Figure 74 (SEQ ID NO:130).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a text DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1244 polypeptide having the sequence of amino acid residues from about 30 to about 335, inclusive of Figure 74 (SEQ ID NO:130), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about an 90% sequence identity, most preferably at least about an 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

in yet another embodiment, the invention concerns agonists and antagonists of a native PRO1244

10 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1244 antibody.

In a further embodiment, the invention concerns a method of identifying agouists or antagonists of a native PRO1244 polypoptide, by contacting the native PRO1244 polypoptide with a candidate molecule and monitoring a biological activity mediated by taid polypoptide.

In a still further embodiment, the invention concerns a composition comprising a PRO 1244 polypeptide.

15 or an agentst or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

PRO1246

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A cDNA clone (DNA64885-1529) has been identified, having bonnology to nucleic acid encoding bone related sulphanase that encodes a novel polypeptide, designated in the present application as "PRO1246".

20 Is one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA exceeding a PRO1246 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1246 polypeptide having 25 the sequence of amino acid residues from about 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID

NO:132), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1246 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 119 or about 164 and about 1726, inclusive, of Figure 75 (SEQ ID NO:121). Preferably, hybridization occurs under 30 stringent hybridization and wash conditious.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203457

35 (DNA64885-1529) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203457 (DNA64885-1529).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO.132), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1246 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO:132), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferrably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated mutleic acid molecule comprising DNA encoding a PRO1246 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 16 in the sequence of Figure 76 (SEQ ID NO:132).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypicptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO:132), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1246 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 73 (SEQ ID NO:131).

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In another embodiment, the invention provides isolated PRO1246 polypeptide encoded by any of the isolated nucleic acid sequences bereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1246 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues I or about 16 to about 536 of Figure 76 (SEO ID NO: 132).

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In another aspect, the invention concerns an isolated PRO1246 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 83% sequence identity, more preferably at least about 93% sequence identity, most preferably at least about 93% sequence identity to the sequence of amino acid residues I or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO:132).

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In a further aspect, the invention concerns an isolated PRO1246 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least

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about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 536, inclusive of Figure 76 (SEQ ID NO:132).

In yet another aspect, the invention concerns an isolated PRO1246 polypeptide, comprising the sequence of amino acid residues 1 or about 16 to about 336, inclusive of Figure 76 (SEQ ID NO:132), or a fragment thereof aufficient to provide a binding site for an anti-PRO1246 antibody. Preferably, the PRO1246 fragment retains a qualitative biological activity of a native PRO1246 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1246 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 336, inclusive of Figure 76 (SEQ ID NO:132), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about a 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) reconvering the polypeptide from the cell culture.

In yet mother embodiment, the invention concerns agonists and antagonists of a native PRO1246 polypoptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1246 ambody.

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In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1246 polypeptide by contacting the native PRO1246 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1246 polypeptide,
or an agonist or antagonist as hereinabove defined, in combination with a pharmacountially acceptable carrier.

39. PRO1356

A cDNA clone (DNA64886-1601) has been identified, having homology to nucleic acid encoding clostridium perfringens enterotoxin teceptor, that encodes a novel polypeptide, designated in the present 25 application as "PRO1356".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO 1356 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most 30 preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1356 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1356 polypeptide comprising DNA hybridizing to the cumplement of the nucleic acid between about nucleotides 122 35 or about 194 and about 811, inclusive, of Figure 77 (SEQ ID NO:133). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity in (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203241 (DNA64886-1601) or (b) the complement of the nucleic neid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203241 (DNA64886-1601).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA carcoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO: 134), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 20 nucleoides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1356 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 230, inchasive of Figure 78 (SEQ ID NO:134), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95 % sequence identity of (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1356 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 14 in the sequence of Figure 78 (SEQ ID NO:134). The transmembrane domains have been tentatively identified as extending from about amino acid position 82 to about amino acid position 102, from about amino acid position 102, from about amino acid position 117 to about amino acid position 140 and from about amino acid position 163 to about amino acid position 182 in the PRO1356 amino acid sequence (Figure 78, SEQ ID NO:124).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO 1356 polypopside coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 77 (SEQ ID NO:133).

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In another embodiment, the invention provides isolated PRO1356 polypeptide encoded by any of the

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isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1356 polypeptide, which in cortain embodiments, includes an amino acid sequence comprising residues 1 or about 25 to about 230 of Figure 78 (SEQ ID NO:134).

In another aspect, the invention concerns an isolated PRO1356 polypeptide, comprising an amino acid

5 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more
preferably at least about 90% sequence identity. most preferably at least about 95% sequence identity to the
sequence of amino acid residues 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134).

In a further aspect, the invention concerns an isolated PRO1356 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134).

In yet another aspect, the invention concerns an isolated PRO1356 polypeptide, comprising the sequence of amino acid residues. 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134), or a fragment thereof sufficient to provide a binding site for an anti-PRO1356 antibody. Preferably, the PRO1356 fragment retains a qualitative biological activity of a native PRO1356 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1356 polypeptide having the sequence of amino acid residues from about 1 or about 25 to about 230, inclusive of Figure 78 (SEQ ID NO:134), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a bost 90% sequence identity, most preferably at least about as 95% sequence identity to (b) or (b), (iii) culturing a bost cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii)

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In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1356
25 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1356 antibody.

recovering the polypeptide from the cell culture.

In a further embodiment, the invention concerns a method of identifying agonists or autagonists of a native PRO1356 polypeptide by contacting the native PRO1356 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition couprising a PRO1356 polypeptide,
or an agentst or antagonist as hereinahove defined, in combination with a pharmaceutically acceptable earnier.

40. PRO127:

A cDNA clone (DNA64888-1542) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1275."

35 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1275 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity

preferably at least about 85% sequence identily, more preferably at least about 90% sequence identily, most preferably at least about 95% sequence identily to (a) a DNA molecule encoding a PRO1275 polypeptide having the sequence of amino acid residues from about 26 to about 119, inclusive of Figure 80 (SEQ ID NO:136), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1275 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 112 and about 393, inclusive, of Figure 79 (SEQ ID NO:135). Preferably, bybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203249 (DNA64888-1542), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203249 (DNA64888-1542).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 26 to about 119, inclusive of Figure 80 (SEQ ID NO:126), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringern conditions with (a) a DNA molecule encoding a PRO1275 polypeptide having the sequence of amino acid residues from about 26 to about 119, inclusive of Figure 80 (SEQ ID NO:136), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about an 85% sequence identity to (a) or (b), isolating the test DNA molecule.

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 26 to about 119, inclusive of Figure 80 (SEQ ID NO:136), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1275 polypeptide coding sequence that may flad use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1275 polypeptide encoded by any of the isolated nucleic acid sequences horeinabove defined.

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In a specific aspect, the invention provides isolated native sequence PRO1275 polypepide, which in one embodiment, includes an amino acid sequence comprising residues 26 through 119 of Figure 80 (SEQ ID NO:136).

In another aspect, the invention concerns an isolated PRO1275 polypepide, comprising an amino acid vequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to the sequence of amino acid residues 26 to about 119, inclusive of Figure 80 (SEQ ID NO:136).

In a further aspect, the invention concerns an isolated PRO1275 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 80% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 26 through 119 of Figure 80 (SEQ ID NO:136).

In yet another aspect, the invention concerns an isolated PRO1275 polypepidle, comprising the sequence of amino acid residues 26 to about 119, inclusive of Figure 80 (SEQ ID NO:136), or a fragment thereof sufficient to provide a binding site for an anti-PRO1275 antibody. Preferably, the PRO1275 fragment remins a qualitative biological activity of a native PRO1275 polypepide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1275 polypeptide having the sequence of amino acid residues from about 26 to about 110, inclusive of Figure 80 (SEQ ID NO:136), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet modure embodiment, the invention concerns agonists and antagonists of a native PRO1275 pulyprptide. In a particular embodiment, the agonist or antagonist is un anti-PRO1275 antibody.

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In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1275 polypeptide, by contacting the native PRO1275 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1275 polypeptide or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

41. PROIZ

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A cDNA clone (DNA64889-1541) has been identified that encodes a novel socreted polypeptide designated in the present application as "PRO1274."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1274 polypeptide.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, more

preferably at least about 95% sequence identity to (a) a DNA molecute encoding a PRO1274 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138) or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1274 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 96 and about 353, inclusive, of Figure 81 (SEQ ID NO:137). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 80% sequence identity in (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203250 (DNA64889-1541), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203250 (DNA64889).

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

15 cnooding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
identity to the sequence of amino acid residues from about 25 to about 110, inclusive of Figure 82 (SEQ ID

NO:138), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1274 polypeptide having the sequence of annho acid residues from about 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity to (a) or (b), isolating the test DNA molecule.

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1274 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1274 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

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In a specific aspect, the invention provides isolated native sequence PRO1274 polypeptide, which in one

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embodiment, includes an amino acid sequence comprising residuca 25 through 110 of Figure 82 (SEQ ID NO:138).

In another aspect, the invention concerns an isolated PRO1274 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138).

In a further aspect, the invention concerns an isolated PRO1774 polypeptide, comprising an amino acid sequence acoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 25 through 110 of Figure 82 (SEQ ID.NO:138).

In yet another aspect, the invention concerns an isolated PRO1274 polypeptide, comprising the sequence of antino acid residues 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138), or a fragment thereof sufficient to provide a binding site for an anti-PRO1274 antibody. Preferably, the PRO1274 fragment retains a qualitative biological activity of a native PRO1274 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

15 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1274 polypeptide having the
sequence of amino acid residues from about 25 to about 110, inclusive of Figure 82 (SEQ ID NO:138), or (b)
the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence
identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about an 95% sequence identity, more preferably at least about an 95% sequence i

In yet another embodiment, the invention concerns againsts and aniagonists of a naive PRO1274 polypeptide. In a particular embodiment, the against or aniagonist is an ani-PRO1274 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a candive PRO1274 polypeptide, by contacting the native PRO1274 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1274 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

42. PRO1412

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A cDNA clone (DNA64897-1628) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1412."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1412 polypeptide.

In one sepect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1412 polypoptide having

the sequence of amino acid residues from 1 or about 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1412 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 226 and about 1074, inclusive, of Figure 83 (SEQ ID NO:139). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203216 (DNA64897-1628), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203216 (DNA64897-1628).

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide baving at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleonides, and preferably at least about 100 nucleonides and produced by hybridizing a test DNA molecule under stringern conditions with (a) a DNA molecule encoding a PRO1412 polypepside having the sequence of amino acid residues from about 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

25
In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1412 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionize, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 28 in the sequence of Figure 84 (SEQ ID NO:140). The transmembrane domain has been rematively identified as extending from about amino acid position 190 through about amino acid position 216 in the PRO1412 amino acid sequence (Figure 84, SEQ ID NO:140).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the autimo acid sequence of residues 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1412 polypeptide coding sequence that may find

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use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1412 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

S In a specific aspect, the invention provides isolated native sequence PRO1412 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 29 to 311 of Figure 84 (SEQ ID NO:140). In another aspect, the invention concerns an isolated PRO1412 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the sequence of amino acid residues 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140).

In a further aspect, the invention concerns an isolated PRO1412 polypeptide, comprising an amino acid sequence scoring at least about 89% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 29 to 311 of Figure 84 (SEQ ID NO:140).

15 In yet another aspect, the invention concerns an isolated PRO1412 polypeptide, comprising the sequence of amino acid residues 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140), or a fragment thereof sufficient to provide a binding site for an anii-PRO1412 antibody. Preferably, the PRO1412 fragment retains a qualitative biological activity of a native PRO1412 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA 20 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1412 polypeptide having the sequence of amino acid residues from about 29 to about 311, inclusive of Figure 84 (SEQ ID NO:140), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising 25 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

43. PRO1557

A cDNA clone (DNA64902-1667) has been identified that encodes a novel polypeptide having homology

30 to chordin and designated in the present application as "PRO1557".

In one embodiment, the invention provides an isolated mucieic acid molecule comprising DNA encoding a PRO1537 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule exceeding a PRO1557 polypeptide having the sequence of amino acid residues from 1 or about 26 to about 451, inclusive of Figure 86 (SEQ ID NO:142), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1557 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 362 and about 1639, inclusive, of Figure 85 (SEQ ID NO:141). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203317 (DNA64902-1667), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203317 (DNA64902-1667).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA cacooding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 26 to about 451, inclusive of Figure 86 (SEQ ID NO:142), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated molecule naving at least about 50 mucleoides, and preferably at least about 100 mucleoides, and produced by bybridizing a test DNA molecule under stringern conditions with (a) a DNA molecule encoding a PRO1557 polypeptide having the sequence of amino acid residues from about 26 to about 451, inclusive of Figure 86 (SEQ ID NO:142), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about at 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1557 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding nucleic acid molecule. The signal peptide has been textualizely identified as extending from amino acid position 1 through about amino acid position 25 in the sequence of Figure 86 (SEQ ID NO:142).

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In another aspect, the invention concerns an bolated nucleic acid motecute comprising (a) DNA encoding a polypoptide scoring at least about 80% positives, preferably at least about 80% positives, more preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 26 to about 451, Inclusive of Figure 86 (SEQ ID NO:142), or (b) the compilement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1557 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 40 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1557 polypeptide encoded by any of the isolated nucleic acid sequences hercinabove defined.

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In a specific aspect, the invention provides toolated native sequence PRO1557 polypepide, which in one embodiment, includes an amino acid sequence comprising residues 26 to 451 of Figure 86 (SEQ ID NO:142).

In another aspect, the invention concerns an isolated PRO1557 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 26 to about 451, inclusive of Figure 86 (SEQ ID NO:142).

In a further aspect, the invention concerns an isolated PRO1557 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, proferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 26 to 451 of Figure 86 (SEQ ID NO:142).

10 In yet another aspect, the invention concerns an isolated PRO1557 polypeptide, comprising the sequence of amino acid residues 26 to about 451, inclusive of Figure 86 (SEQ ID NO:142), or a fragment thereof sufficient to provide a binding site for an anti-PRO1557 antibody. Preferably, the PRO1557 fragment retains a qualitative biological activity of a native PRO1557 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

15 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1557 polypeptide having the
sequence of amino acid residues from about 26 to about 451, inclusive of Figure 86 (SEQ ID NO:142), or (b)
the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence
identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising

20 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the
polypeptide from the cell culture.

In yet another embodiment, the Invention concerns agonists and antagonists of a native PRO1557 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1557 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a 25 native PRO1557 polypeptide by contacting the native PRO1557 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

in a still further embodiment, the invention concerns a composition comprising a PRO1557 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaccutically acceptable carrier.

30 44. PRO128

A cDNA clone (DNA64903-1553) has been identified that encodes a novel secreted polypeptide that is designated in the present application as "PRO1286."

la one embodiment, the invention provides an isolated matlete acid molecule comprising DNA encoding a PRO1286 not mentide.

35 In one aspect, the isolated nucleic acid comprites DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1286 polypeptide having preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1286 polypeptide having

the sequence of anino axid residues from 1 or about 19 to about 93, inclusive of Figure 88 (SEQ ID NO:144) or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1286 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 147 and about 371, inclusive, of Figure 87 (SEQ ID NO:143). Preferably, hybridization occurs under stringen hybridization and west conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203223 (DNA64903-1553), or (b) the cumplement of the DNA molecule of (a). In a preferred embodiment, the macheic acid comprises a DNA encoding the same mature polypeptide of the DNA molecule of (b). In a preferred embodiment, the macheic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203223 (DNA64903-1553).

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 93, inclusive of Figure 88 (SEQ ID NO:144), or the complement of the DNA of (a).

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In a further aspect, the Invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1286 polypeptide having the sequence of amino acid residues from about 19 to about 93, inclusive of Figure 88 (SEQ ID NO:144), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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25 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO 1286 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from antino acid position 1 through about amino acid position 18 in the sequence of Figure 88 (SEQ ID NO:144).

30 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA emoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to about 95, inclusive of Figure 88 (SEQ ID NO:144), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1286 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50

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nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1286 polypeptide encode

In another embodiment, the invention provides isolated PRO1286 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1286 polypapide, which in one embodiment, includes an amino acid sequence comprising residues 19 to 93 of Figure 88 (SEQ ID NO:144).

In another aspect, the invention concerns as isolated PRO11106 concerns as

In another aspect, the invention concerns an isolated PRO1286 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 95, inclusive of Figure 88 (SEQ ID NO:144).

In a further aspect, the invention concerns an isolated PRO 1286 polypeptide, comprising an amino acid

10 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least
about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence
of residues 19 to 93 of Figure 88 (SEQ ID NO:144).

In yet another aspect, the invention concerns an isolated PRO1286 polypeptide, comprising the sequence of amino acid residues 19 to about 93, inclusive of Figure 88 (SEQ ID NO:144), or a fragment thereof sufficient 15 to provide a binding site for an anti-PRO1286 antibody. Preferably, the PRO1286 fragment retains a qualitative biological activity of a native PRO1286 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1286 polypeptide having the sequence of amino acid residues from about 19 to about 93, inclusive of Figure 88 (SEQ ID NO:144), or (b) 20 the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

45. PROJ294

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A cDNA clone (DNA64905-1558) has been identified, having homology to nucleic acid encoding offsetomedin, that encodes a novel polypeptide, designated in the present application as "PRO1294".

In one embodiment, the invention provides an Isolated nucleic acid molecule comprising DNA encoding a PRO1294 polypeptide.

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In one aspect, the isolated nucleic axid comprises DNA having at least about 80% sequence identity, preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1294 polypeptide having the sequence of amino acid residues from about 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID 35 NO:146), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated modelo acid molecule encoding a PRO1294 polypeptide comprising DNA hybridizing to the complement of the modelo acid between about nucleotides 110

or about 173 and about 1327, inclusive, of Figure 89 (SEQ ID NO:145). Preferably, hybridization occurs under stringent hybridization and wash conditions.

encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203233 ATCC Deposit No. 203233 (DNA64905-1558). (DNA64905-1558) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least in a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence NO:146), or (b) the complement of the DNA of (a). identity to the sequence of amino acid residues 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID identity, more preferably at least about 90% acquence identity, most preferably at least about 95% sequence In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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identity to (a) or (b), isolating the test DNA molecule. nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence about 406, inclusive of Figure 90 (SEQ ID NO:146), or (b) the complement of the DNA molecule of (a), and molecule encoding a PRO1294 polypeptide having the sequence of amino acid residues from 1 or about 22 to identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10

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a PRO1294 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is extending from about amino acid position I to about amino acid position 21 in the sequence of Figure 90 (SEQ complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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the complement of the DNA of (a). preferably at least about 90% positives, most preferably at least about 95% positives when compared with the encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more ımino acid sequence of residues 1 or about 22 to about 406, inchusive of Figure 90 (SEQ ID NO:146), or (b) In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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from the nucleotide sequence shown in Figure 89 (SEQ ID NO:145). preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, ucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived Another embodiment is directed to fragments of a PRO 1294 polypeptide coding sequence that may find

isolated nucleic acid sequences hereinabove identified. In another embodiment, the invention provides isolated PRO1294 polypeptide encoded by any of the ᇇ

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certain embodiments, includes an ammo acid sequence comprising residues 1 or about 22 to about 406 of Figure In a specific aspect, the invention provides isolated native sequence PRO1294 polypeptide, which in

Ui preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID NO:146). sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more In another supect, the invention concerns an isolated PRO1294 polypeptide, comprising an amino acid

ö of residues 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID NO:146). sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence In a further aspect, the invention concerns an isolated PRO1294 polypeptide, comprising an amino acid

of amino acid residues 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID NO:146), or a fragment thereof sufficient to provide a binding site for an anti-PRO1294 antibody. Preferably, the PRO1294 fragment remins a qualitative biological activity of a native PRO1294 polypeptide. In yet another aspect, the invention concerns an isolated PRO1294 polypeptide, comprising the sequence

- 20 15 in a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA
- 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a recovering the polypeptide from the cell culture. NO:146), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about sequence of amino acid residues from about 1 or about 22 to about 406, inclusive of Figure 90 (SEQ ID molecule under stringem conditions with (a) a DNA molecule encoding a PRO1294 polypeptide baving the
- polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1294 antibody. In yet mother embodiment, the invention concerns agonists and antagonists of a native PRO1294
- ß native PRO1294 polypeptide by contacting the native PRO1294 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide. In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

or an agonist or amagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO 1294 polypeptide.

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identity with butyrophilin and designated in the present application as "PRO1347." A cDNA clone (DNA64950-1590) has been identified that encodes a novel polypeptide having sequence

a PRO1347 polypeptide. In one embodiment, the invention provides an isolated meteix acid molecule comprising DNA encoding

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preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1347 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 500, inclusive of Figure 92 (SEQ ID NO:148) or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1347 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 234 and about 1682, inclusive, of Figure 91 (SEQ ID NO:147). Preferably, hybridization occurs under stringent

hybridization and wash conditions.

In a further expect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, most preferably at least about 85% sequence identity in (a) a DNA molecule euroding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203224 (DNA64950-1590), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203224 (DNA64950-1590).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

15 encoding a polypeptide baving at least about 80% sequence identity, preferably at least about 85% sequence
identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
identity to the sequence of amino acid residues from about 18 to about 500, inclusive of Figure 92 (SEQ ID

NO:148), or the complement of the DNA of (a).

In a further aspect, the invention concerns an stolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1347 polypeptide having the sequence of amino acid residues from about 18 to about 500, inclusive of Figure 92 (SEQ ID NO:148), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 80% sequence identity, most preferably at least about a 90% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1347 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted (or that terminus truncated) or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tenatively identified as extending from amino acid position I through about amino acid position 17 in the sequence of Figure 92 (SEQ ID NO:148). The transmembrane domain has been tenatively identified as extending from about amino acid position 239 through about amino acid position 235 in the PRO1347 amino acid sequence (Figure 92, SEQ ID NO:148).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 18 to about 500, inclusive of Figure 92 (SEQ ID NO:148), or (b) the

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complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1347 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embudiment, the invention provides isolated PRO1347 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1347 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 18 through 500 of Figure 92 (SEQ ID NO:148).

10 In another aspect, the invention concerns an isolated PRO1347 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence (dentity to the sequence of amino acid residues 18 to about 500, inclusive of Figure 92 (SEQ ID NO:148).

In a further aspect, the invention concerns an isolated PRO1347 polypeptide, comprising an amino acid

15 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 18 through 500 of Figure 92 (SEQ ID NO:148).

In yet another aspect, the invention concerns an isolated PRO1347 polypeptide, comprising the sequence of amino acid residues 18 to about 500, inclusive of frigure 92 (SEQ ID NO:148), or a fragment ficreof 20 sufficient to provide a binding site for an anti-PRO1347 antibody. Preferably, the PRO1347 fragment retains a qualitative biological activity of a native PRO1347 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1347 polypeptide having the sequence of amino acid residues from about 18 to about 500, inclusive of Figure 92 (SEQ ID NO:148), or (b) 25 the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

30 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1347 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1347 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1347 polypeptide, by contacting the native PRO1347 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

35 In a still further embodiment, the invention concerns a composition comprising a PRO1347 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

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designated in the present application as "PRO1305". A cDNA clone (DNA64952-1568) has been identified that encodes a novel accreted polypeptide

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

- NO:153), or (b) the complement of the DNA molecule of (a). the sequence of amino acid residues from about 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1305 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity.
- 5 or about 201 and about 899, inclusive, of Figure 93 (SEQ ID NO:152). Preferably, hybridization occurs under polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 126 stringent hybridization and wash conditions In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1305

15 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least ATCC Deposit No. 203222 (DNA64952-1568). nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in (DNA64932-1568) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the encoding the same mature polypeptide encoded by the human proxein cDNA in ATCC Deposit No. 203222 about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

NO:153), or (b) the complement of the DNA of (a). identity to the sequence of amino acid residues 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence about 238, inclusive of Figure 94 (SEQ ID NO:153), or (b) the complement of the DNA molecule of (a), and, identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence molecule encoding a PRO1305 polypeptide having the sequence of amino acid residues from 1 or about 26 to nucleotides and produced by hybridizing a test DNA molecule under stringem conditions with (a) a DNA identity to (a) or (b), isolating the test DNA molecule. In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10

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complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as a PRO1305 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is extending from about amino acid position I to about amino acid position 25 in the sequence of Figure 94 (SEQ In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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the complement of the DNA of (a). preferably at least about 90% positives, most preferably at least about 95% positives when compared with the encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more amino acid sequence of residues I or about 26 to about 258, inclusive of Figure 94 (SEQ ID NO:153), or (b) In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

- from the nucleotide sequence shown in Figure 93. (SEQ ID NO:152). nucleorides in length and most preferably from about 20 to about 40 nucleorides in length and may be derived preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, Another embodiment is directed to fragments of a PRO1305 polypeptide coding sequence that may find
- ö isolated nucleic acid sequences hereinabove identified. In another embodiment, the invention provides isolated PRO1305 polypeptide encoded by any of the

certain embodiments, includes an amino acid sequence comprising residues 1 or about 26 to about 258 of Figure In a specific aspect, the invention provides isolated native sequence PRO1305 polypeptide, which in

- sequence of amino acid residues 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID NO:153). preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more In another aspect, the invention concerns an isolated PRO1305 polypeptide, comprising an amino acid
- 20 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least of residues 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID NO:153). about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence In a further aspect, the invention concerns an isolated PRO1305 polypeptide, comprising an amino acid
- 23 thereof sufficient to provide a binding site for an anti-PRO1305 antibody. Preferably, the PRO1305 fragment of amino acid residues 1 or about 26 to about 238, inclusive of Figure 94 (SEQ ID NO:153), or a fragment retains a qualitative biological activity of a narive PRO1305 polypeptide. In yet another aspect, the invention concerns an isolated PRO1305 polypeptide, comprising the sequence
- NO:133), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about molecule under stringent conditions with (a) a DNA molecule encoding a PRO1305 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 258, inclusive of Figure 94 (SEQ ID In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DN/
- છ cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a hos an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a recovering the polypoptide from the cell culture

8. PRO1273

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A cDNA cloue (DNA65402-1540) has been identified that encodes a novel polypeptide having sequence

identity with lipocalins and designated in the present application as "PRO1273."

In one embodimem, the invention provides an isolated nucleic acid molecule comprising DNA encoding

preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1273 polypeptide having or (b) the complement of the DNA molecule of (a). the sequence of amino acid residues from 1 or about 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158), preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

hybridization and wash conditions. about 514, inclusive, of Figure 95 (SEQ ID NO:157). Preferably, hybridization occurs under stringent polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 86 and In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1273

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encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203252 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least Deposit No. 203252 (DNA65402-1540). acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC (DNA65402-1540), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

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20 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence NO:158), or the complement of the DNA of (a). identity to the sequence of amino acid residues from about 21 to about 163, inclusive of Figure 96 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, amino acid residues from about 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158), or (b) the under stringent conditions with (a) a DNA molecule encoding a PRO1273 polypeptide having the sequence of In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

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complement of the DNA of (a). amino acid sequence of residues 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158), or (b) the preferably st least about 90% positives, most preferably at least about 95% positives when compared with the encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, Another embodiment is directed to fragments of a PRO1273 polypeptide coding sequence that may find 33

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nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length. preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50

isolated nucleic acid sequences hereinabove defined in another embodiment, the invention provides isolated PRO1273 polypeptide encoded by any of the

embodiment, includes an animo acid sequence comprising residues 21 through 163 of Figure 96 (SEQ ID NO:158). In a specific aspect, the invention provides isolated native sequence PRO1273 polypeptide, which in one

10 sequence of amino acid residues 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158). preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more In another aspect, the invention concerns an isolated PRO1273 polypeptide, comprising an amino acid

of residues 21 through 163 of Figure 96 (SEQ ID NO:158). about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated PRO1273 polypeptide, comprising an amino acid

15 of amino acid residues 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158), or a fragment thereof a qualitative biological activity of a native PRO1273 polypeptide. sufficient to provide a binding site for an anti-PRO1273 antibody. Preferably, the PRO1273 fragment retains In yet another aspect, the invention concerns an isolated PRO1273 polypeptide, comprising the sequence

23 20 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the molecule under stringent conditions with (a) a DNA molecule encoding a PRO1273 polypeptide having the polypeptide from the cell culture. identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence sequence of amino acid residues from about 21 to about 163, inclusive of Figure 96 (SEQ ID NO:158), or (b) In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DN/

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1273 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1273

30 native PRO1273 polypeptide, by contacting the native PRO1273 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide. In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carries In a still further embodiment, the invention concerns a composition comprising a PRO1273 polypeptide

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identity with CD33 and designated in the present application as "PRO1302." A cDNA clone (DNA65403-1565) has been identified that encodes a novel polypeptide having sequence

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1302 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1302 polypeptide having the sequence of amino acid residues from 1 or about 15 to about 463, inclusive of Figure 98 (SEQ ID NO:160), or (b) the complement of the DNA molecule of (a).

th another expect, the invention concerns an isolated nucleic acid molecule encoding a PRO1302 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 88 and about 1431, inclusive, of Figure 97 (SEQ ID NO:159). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203230 (DNA6S403-1565), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the molecule comprises a DNA encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203230 (DNA6S403-1565).

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, on the sequence of amino acid residues from about 16 to about 463, inclusive of Figure 98 (SBQ ID NO:160), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule 25 under stringent conditions with (a) a DNA molecule encoding a PRO1302 polypeptide having the sequence of amino acid residues from about 16 to about 463, inclusive of Figure 98 (SEQ ID NO:160), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), itsolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1302 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted (or truncated form) or hactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 15 in the sequence of Figure 98 (SEQ ID NO:160). The transmembrane domain has been tentatively identified as extending from about amino acid position 351 through about amino acid position 370 in the PRO1302 amino acid sequence (Figure 98, SEQ ID NO:169).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DN/

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encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to about 463, inclusive of Figure 98 (SEQ ID NO:160), or (b) the complement of the DNA of (a).

Azouber embodiment is directed to fragments of a PRO1302 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1202 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

10 In a specific aspect, the invention provides isolated native sequence PRO1302 polypeptide, which in one embodiment, includes an amino seid sequence comprising residues 16 through 463 of Figure 98 (SEQ ID NO:160).

In another aspect, the invention concerns an isolated PRO1302 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more 15 preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 16 to about 463, inclusive of Figure 98 (SEQ ID NO:160).

In a further aspect, the invention concerns an isolated PRO1302 polypeptide, comprising an amino acid sequence souring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 80% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence 20 of residues 16 through 463 of Figure 98 (SEQ ID NO:160).

In yet another aspect, the invention concerns an isolated PRO1302 polypeptide, comprising the sequence of amino acid residues 16 to about 465, inclusive of Figure 98 (SEQ ID NO:160), or a fragment thereof sufficient to provide a binding site for an anti-PRO1302 antibody. Preferably, the PRO1302 fragment retains a qualitative biological activity of a native PRO1302 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1302 polypeptide having the sequence of amino acid residues from about 16 to about 463, inclusive of Figure 98 (SEQ ID NO:160), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable (or expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1302 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1302 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or anagonists of a native PRO1302 polypeptide, by contacting the native PRO1302 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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or an agonist or antagonist as herninabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invention concerts a composition comprising a PRO 1302 polypeptide

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a PRO1283 polypeptide. odorant binding protein, that encodes a novel polypeptide, designated in the present application as "PRO1283" A cDNA clone (DNA65404-1551) has been identified, having homology to nucleic acid encoding In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1283 polypeptide having NO:162), or (b) the complement of the DNA molecule of (a). the sequence of amino acid residues from about 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, mos In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity

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or about 96 and about 554, inclusive, of Figure 99 (SEQ ID NO:161). Preferably, hybridization occurs under stringent hybridization and wash conditions polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 45 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1283

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20 encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203244 ATCC Deposit No. 203244 (DNA65404-1551). nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in (DNA65404-1551) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least In a further aspect, the invention concerns an isolated nucleic acid molecute comprising DNA having

z identity to the sequence of animo acid residues 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence NO:162), or (b) the complement of the DNA of (a). identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

35 identity to (a) or (b), isolating the test DNA molecule. nucleorides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA If the DNA molecule has at least about an 80% sequence identity, prefereably at least about an 85% sequence about 170, inclusive of Figure 100 (SEQ ID NO:162), or (b) the complement of the DNA molecule of (a), and molecule encoding a PRO1283 polypeptide having the sequence of amino acid residues from 1 or about 18 to dentity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10

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a PRO1283 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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extending from about amino acid position I to about amino acid position 17 in the sequence of Figure 100 (SEQ complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as

preferably at least about 90% positives, most preferably at least about 95% positives when compared with the emoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more the complement of the DNA of (a). amino acid sequence of residues 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID NO:162), or (b) In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

10 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, from the nucleotide sequence shown in Figure 99 (SEQ ID NO:161). sucleotides in length and most preferably from abous 20 to abous 40 nucleotides in length and may be derived Another embodiment is directed to fragments of a PRO1283 polypeptide coding sequence that may find

isolated nucleic acid sequences hereinabove identified. In another embodiment, the invernion provides isolated PRO1283 polypeptide encoded by any of the

5 100 (SEQ ID NO:162). certain embodiments, includes an amino acid sequence comprising residues 1 or about 18 to about 170 of Figure In a specific aspect, the invention provides isolated native sequence PRO1283 polypeptide, which in

20 preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID NO:162). sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more In another aspect, the invention concerns an isolated PRO1283 polypeptide, comprising an amino acid

23 of residues 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID NO:162). about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated PRO1283 polypeptide, comprising an amino acid

of amino acid residues 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID NO:162), or a fragment retains a qualitative biological activity of a native PRO1283 polypeptide. thereof sufficient to provide a binding site for an anti-PRO1283 antibody. Preferably, the PRO1283 fragment In yet another aspect, the invention concerns an isolated PRO1283 polypeptide, comprising the sequence

35 30 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host molecule under stringent conditions with (a) a DNA molecule encoding a PRO1283 polypeptide having the recovering the polypeptide from the cell culture cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) un 80% sequence identity, preferably at least ahout an 85% sequence identity, more preferably at least about a NO:162), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about sequence of amino acid residues from about 1 or about 18 to about 170, inclusive of Figure 100 (SEQ ID In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

In yet another embodiment, the invention concerts agonists and anagonists of a native PRO1282 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1283 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1283 polypeptide by contacting the native PRO1283 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO 1283 polypeptide, or an agentist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

51. PRO127

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A cDNA clone (DNA65405-1347) has been identified, having homology to nucleic acid encoding neuropsin that encodes a novel polypeptide, designated in the present application as "PRO1279".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1279 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encotting a PRO1279 polypeptide having the sequence of amino acid residues from about 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1279 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleoxides 106 or about 160 and about 855, inclusive, of Figure 101 (SEQ ID NO:169). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203476 (DNA65405-1547) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203476 (DNA65405-1547).

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In still a further aspect, the invention concerns an isolated nucleic axid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, to the sequence of amino acid residues 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleorides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1279 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170), or (b) the complement of the DNA molecule of (a), and,

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if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

a PRO1279 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been ternatively identified as extending from about amino acid position 1 to about amino acid position 18 in the sequence of Figure 102 (SEQ ID NO:170).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 80% positives, more 10 preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1279 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length.

15 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence abown in Figure 101 (SEQ ID NO:169).

In another embodiment, the invention provides isolated PRO1279 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

20 In a specific aspect, the invention provides isolated native sequence PRO1279 polypopaide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 19 to about 250 of Figure 102 (SEQ ID NO:170).

In another aspect, the invention concerns an isolated PRO1279 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity in the sequence of amino acid residues 1 or about 190 to about 250, inclusive of Figure 102 (SEQ ID NO:170).

In a further expect, the invention concerns an isolated PRO 1279 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence

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of residues 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170).

In yet another aspect, the invention concerns an isolated PRO1279 polyeptide, comprising the sequence of amino acid residues 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID NO:170), or a fragment thereof sufficient to provide a binding site for an anti-PRO1279 antibody. Preferably, the PRO1279 fragment retains a qualitative biological activity of a native PRO1279 polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringem conditions with (a) a DNA molecule encoding a PRO1279 polypeptide having the sequence of amino acid residues from about 1 or about 19 to about 250, inclusive of Figure 102 (SEQ ID).

NO:170), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about an 85% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the tell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1279 polypeptide. In a particular embodiment, the agonist or antagonist is an ami-PRO1279 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or anagomists of a native PRO1279 polypeptide by contacting the native PRO1279 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1279 polypeptide, or an agonist or an agonist as hereimabove defined, in combination with a pharmaceutically acceptable carrier.

52. PRO1304

A cDNA clone (DNA65406-1567) has been identified, having homology to nucleic acid encoding FK566

15 binding protein that encodes a novel polypeptide, designated in the present application as "PRO1304".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1304 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to (a) a DNA molecule encoding a PRO 1304 polypeptide having the sequence of amino acid residues from about 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1304 polypeptide comprising DNA hybridizing to the complement of the mucleic acid between about mucleotides 23 and about 688, inclusive, of Figure 103 (SEQ ID NO:179). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203219 (DNA65406-1567) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203219 (DNA65406-1567).

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In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, on the sequence of amino acid residues 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180), or

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(b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1304 polypopriste having the sequence of amino acid residues from 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180), or (b) the complement of the DNA molecule of (a), and, if the DNA nolecule has at least about an 80 % sequence identity, preferrably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity in most preferably at least about a 90 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1904 polypeptide, with or without the initiating methionine, or is complementary to such encoding nucleic acid molecule.

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO 1304 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 103 (SEQ ID NO.179).

In another embodiment, the invention provides isolated PRO1304 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

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In a specific aspect, the invention provides isolated native sequence PRO1304 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues I to about 222 of Figure 104 (SEQ 25 ID NO:180).

In another aspect, the invention concerns an isolated PRO1304 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of antino acid residues 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180).

In a further aspect, the invention concerns an isolated PRO 1304 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 222, inclusive of Figure 104 (SEQ ID NO: 180).

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In yet another aspect, the liveration concerns an isolated PRO1304 polypeptide, comprising the sequence of amino acid residues 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180), or a fragment thereof sufficient to provide a binding site for an anti-PRO1304 antibody. Preferably, the PRO1304 fragment retains a qualitative biological activity of a native PRO1304 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1304 polypeptide having the sequence of amino acid residues from about 1 to about 222, inclusive of Figure 104 (SEQ ID NO:180), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity on (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1304 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1304 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1304 polypeptide by contacting the native PRO1304 polypeptide with a candidate molecule and monitoring a biological activity moditated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO1304 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier,

PR01317

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A cDNA clone (DNA65408-1578) has been identified that encodes a novel secreted polypeptide that shares homology with human CD97. The novel polypeptide is designated in the present application as "PRO1317".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO 1317 polypeptide.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1317 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1317 polypepide comprising DNA hybridizing to the complement of the nucleic acid between about residues 60 and about 227, inclusive, of Figure 105 (SEQ ID NO:188). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% requence identity, preferably at least about 80% requence identity, more preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to (a) a DNA molecule encoding the same mature polypoptide encoded by the human protein cDNA in ATCC Deposit No. 203217 (DNA6408:1578), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypoptide encoded by the human protein cDNA in ATCC

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1317 polypeptide having the sequence of amino acid residues from about 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1317 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 18 in the sequence of Figure 106 (SEQ ID NO:189).

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In mother aspect, the invention concerns an isolated methic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1317 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1317 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1317 polypeptide, which in one

embodiment, includes an amino acid sequence comprising residues 19 to 74 of Figure 106 (SEQ ID NO:189).

In another aspect, the invention concerns an isolated PRO1317 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to the sequence of amino acid residues 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189).

In a further aspece, the invention concerns an isolated PRO 1317 polypeptide, comprising an amino acid

35 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least
about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence
of residues 19 to 74 of Figure 106 (SEQ ID NO:189).

In yet another aspect, the invention concerns an isolated PRO1317 polypeptide, comprising the sequence of amino acid residues 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189), or a fragment thereof sufficient to provide a binding site for an anti-PRO1317 antibody. Preferably, the PRO1317 fragment retains a qualitative biological activity of a native PRO1317 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1317 polypeptide having the sequence of amino acid residues from about 19 to about 74, inclusive of Figure 106 (SEQ ID NO:189), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity of (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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54. PKO1303

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A cDNA clone (DNA65409-1566) has been identified that encodes a novel polyceptide having sequence identity with protesses including neuropsin and designated in the present application as "PRO1303."

In one embodiment, the invention provides an isolated meleic acid molecule comprising DNA encoding a PRO 1303 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1303 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 248, inclusive of Figure 108 (SEQ ID NO:194), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1303 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 172 and about 864, inclusive, of Figure 107 (SEQ ID NO:193). Preferably, hybridization occurs under stringent bybridization and wash conditions.

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In a further expect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity to (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203232 (DNA65409-1566), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, once preferably at least about 90% sequence identity, once preferably at least about 90% sequence identity, once preferably at least about 90% sequence.

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NO:194), or the complement of the DNA of (a).

in a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1303 polypeptide having the sequence of amino acid residues from about 18 to about 248, inclusive of Figure 108 (SEQ ID NO.194), or (b) the 5 complement of the DNA molecule of (a), and, if the DNA molecule has at least about a 90% sequence identity, preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more 10 preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 18 to about 24%, inclusive of Figure 108 (SEQ ID NO:194), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1303 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleoides in length.

15 preferably from about 20 to about 60 nucleoides in length, more preferably from about 20 to about 50 nucleoides in length, and most preferably from about 20 to about 40 nucleoides in length.

In another embodiment, the invention provides isolated PRO1303 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1303 polypeptide, which in one
20 embodiment, includes an amino acid sequence comprising residues 18 through 248 of Figure 108 (SEQ ID
NO:194).

In another aspect, the invention concerns an isolated PRO 1303 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the preferably at least about 95% sequence identity to the preferably at least about 95% sequence identity to the preferably at least about 95% sequence identity to the preferably at least about 95% sequence identity to the preferably at least about 95% sequence identity to the preferably at least about 95% sequence identity to the preferably at least about 95% sequence identity.

In a further aspect, the invention concerns an isolated PRO1303 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 188 through 248 of Figure 108 (SEQ ID NO:194).

30 In yet another aspect, the invention concerns an isolated PRO1303 polypeptide, comprising the sequence of antino acid residues 18 to about 248, inclusive of Figure 108 (SEQ ID NO:194), or a fragment thereof sufficient to provide a binding site for an ami-PRO1303 antihody. Preferably, the PRO1303 fragment retains a qualitative biological activity of a native PRO1303 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

35 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1303 polypeptide having the
sequence of amino acid residues from about 18 to about 248, inclusive of Figure 108 (SEQ ID NO:194), or (b)
the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence

identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

in yet another embodinent, the invention concerns agonists and anagonists of a native PRO1303 polypeptide. In a particular embodinent, the agonist or anagonist is no noti-PRO1303 antibody.

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In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1303 polypeptide, by contacting the native PRO1303 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

ha still further embodiment, the invention concerns a composition comprising a PRO 1303 polypeptide or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

55. PRO1300

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A cDNA clone (DNA65410-1569) has been identified that encodes a novel polypeptide having homology to AIFI/daintain and designated in the present application as "PRO1306".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1306 polypeptide.

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In one aspect, the isolated meleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to (a) a DNA molecule encoding a PRO1306 polypeptide having the sequence of amino acid residues from about 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1306 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 106 and about 555, inclusive, of Figure 109 (SEQ ID NO:195). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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in a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203231

30 (DNA65410-1569), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203231 (DNA65410-1569).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypoptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1306 polypeptide having the sequence of amino acid residues from about 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In another aspect, the invention concerns in isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the 10 amino acid sequence of residues 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1306 polypeptide coding sequence that may find use as hybridization probes. Such mucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO 1306 polypeptide encoded by any of the isolated nucleic acid acquences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1306 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 150 of Figure 110 (SEQ ID NO:196).

In mother aspect, the invention concerns an isolated PRO 1306 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of animo acid residues 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196).

In a further aspect, the invention concerns an isolated PRO1306 polypeptide, comprising an amino acid

25 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 150 of Figure 110 (SEQ ID NO:196).

In yet another aspect, the invention concerns an isolated PRO1306 polypeptide, comprising the sequence of amino acid residues 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196), or a fragment thereof 30 sufficient to provide a binding site for an anti-PRO1306 antibody. Preferably, the PRO1306 fragment retains a qualitative biological activity of a native PRO1306 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1306 polypeptide having the sequence of amino acid residues from about 1 to about 150, inclusive of Figure 110 (SEQ ID NO:196), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 80% sequence identity, more preferably at least about a 80% sequence identity, more preferably at least about a 80% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising

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the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1306 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1306 antibody.

In a further embodiment, the invention concerns a method of identifying agentists or antagonists of a native PRO1306 polypeptide, by contacting the native PRO1306 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1306 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable currier

10 ss. PRO1336

A cDNA clone (DNA65423-1595) has been identified that encodes a novel polypeptide having sequence identity with slit and designated in the present application as "PRO1336."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1336 polypeptide.

- In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1336 polypepide having the sequence of amino acid residues from 1 or about 28 to about 1523, inchasive of Figure 112 (SEQ ID NO:198), or (b) the complement of the DNA molecule of (a).
- In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1336 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between shout residues 164 and about 4651, inclusive, of Figures 111A-B (SEQ ID NO:197). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203227 (DNA6S423-1595), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203227 (DNA6S423-1595).

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In a still further aspect, the invention concerns an isolated nucleit acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of arnino acid residues from about 28 to about 1523, inclusive of Figure 112 (SEQ ID NO:198), or the complement of the DNA of (a).

in a Aurther aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule

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under stringent conditions with (a) a DNA molecute encoding a PRO1336 polypeptide having the sequence of amino acid residnes from about 28 to about 1523, inclusive of Figure 112 (SEQ ID NO:198), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about a 80% sequence identity, preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), itolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 28 to about 1523, inclusive of Figure 112 (SEQ ID NO:198), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1336 polypeptide coding sequence that may find use at hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1336 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

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In a specific aspect, the invention provides isolated native sequence PRO1336 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 28 through 1523 of Figure 112 (SEQ ID NO:198).

In another aspect, the invention concerns an isolated PRO1336 polypeptide, comprising an amino acid
20 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more
preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
sequence of amino acid residues 28 to about 1523, inclusive of Figure 112 (SEQ ID NO:198).

In a further aspect, the invention concerns an isolated PRO1336 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 28 through 1523 of Figure 112 (SEQ ID NO:198).

In yet another aspect, the invention concerns an isolated PRO1336 polypeptide, comprising the sequence of amino acid residues 28 to about 1523, inclusive of Figure 112 (SEQ ID NO:198), or a fragment thereof sufficient to provide a binding site for an anti-PRO1336 antibody. Preferably, the PRO1336 fragment retains 30 a qualitative biological activity of a native PRO1336 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a rest DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1336 polypeptide having the sequence of amino acid residues from about 28 to about 1523, Inclusive of Figure 112 (SEQ ID NO:198), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii)

recovering the polypeptide from the cell culture

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1336 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1336 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or anagonists of a native PRO1336 polypeptide, by contacting the native PRO1336 polypeptide with a candidate molecule and murnituring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1336 polypeptide, or an agonist or antagonist as bereinabove defined, in combination with a pharmaceutically acceptable carrier.

57. PRO127

A cDNA clone (DNA66304-1546) has been identified that encodes a novel polypeptide having homology to lysozyme C and designated in the present application as "PRO1278."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding RO1278 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, most preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1278 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1278

20 polypoptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 198 and about 584, inclusive, of Figure 113 (SEQ ID NO.202). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 89% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203321 (DNA66394-1546), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203321 (DNA66394-1546).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, one preferably at least about 95% sequence identity, one to the complement of the DNA of (a).

NO:203), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1278 polypeptide having the sequence of

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amino acid residues from abour 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity in (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1278 polypepide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding mucleic acid molecule. The signal peptide has been tenuntively identified as extending from amino acid position 1 through about amino acid position 19 in the sequence of Figure 114 (SEQ ID NO.203).

In another aspect, the invention concerns an Isolated nucleic acid molecule comprising (a) DNA

10 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
amino acid sequence of residues 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203), or (b) the
complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1278 polypeptide ending sequence that may find
15 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1278 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1278 polypepide, which in one embodiment, includes an amino acid sequence comprising residues 20 to 148 of Figure 114 (SEQ ID NO:203).

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In another aspect, the invention concerns an isolated PRO1278 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203).

In a further aspect, the invention concerns an isolated PRO1278 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 20 to 148 of Figure 114 (SEQ ID NO:203).

In yet another aspect, the invention concerns an isolated PRO1278 polypeptide, comprising the sequence of amino acid residues 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203), or a fragment thereof sufficient to provide a binding site for an anti-PRO1278 antibody. Preferably, the PRO1278 fragment retains a qualitative biological activity of a native PRO1278 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA soliceule under stringent conditions with (a) a DNA molecule encoding a PRO1278 polypeptide having the sequence of amino acid residues from about 20 to about 148, inclusive of Figure 114 (SEQ ID NO:203), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence

polypeptide from the cell culture. the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1278 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1278

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monitoring a biological activity mediated by said polypeptide. native PRO1278 polypeptide, by contacting the native PRO1278 polypeptide with a candidate molecule and In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

or an agonist or antagonist as hereinabove defined, in combination with a pharmaccutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO1278 polypeptide.

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identity with glycosyltransferases and designated in the present application as "PRO1298." A cDNA clone (DNA66511-1563) has been identified that encodes a novel polypeptide having sequence

a PRO1298 polypeptide. In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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or (b) the complement of the DNA molecule of (a). the sequence of amino acid residues from 1 or about 16 to about 323, inclusive of Figure 116 (SEQ ID NO:210), preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1298 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

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hybridization and wash conditions. polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 139 and about 1062, inclusive, of Figure 115 (SEQ ID NO:209). Preferably, hybridization occurs under stringent In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1298

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(DNA66511-1563), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203228 about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

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Deposit No. 203228 (DNA66511-1563).

identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 16 to about 323, inclusive of Figure 116 (SEQ ID encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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NO:210), or the complement of the DNA of (a).

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preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (h), isolating the test DNA molecule. complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity. amino acid residues from about 16 to about 323. inclusive of Figure 116 (SEQ ID NO:210), or (b) the under stringent conditions with (a) a DNA molecule encoding a PRO1298 polypeptide having the sequence of nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

10 amino acid sequence of residues 16 to about 323, inclusive of Figure 116 (SEQ ID NO:210), or (b) the complement of the DNA of (a). preferably at least about 90% positives, most preferably at least about 95% positives when compared with the encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length. preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 use as hybridization probes. Such nucleic acid fragments are from about 20 to ahout 80 nucleotides in length Another embodiment is directed to fragments of a PRO1298 polypeptide coding sequence that may find

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isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated PRO1298 polypeptide encoded by any of the

embodiment, includes an amino acid sequence comprising residues 16 through 323 of Figure 116 (SEQ ID In a specific aspect, the invention provides isolated native sequence PRO1298 polypeptide, which in one

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sequence of amino acid residues 16 to about 323, inclusive of Figure 116 (SEQ ID NO:210). sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the In another aspect, the invention concerns an isolated PRO 1298 polypeptide, comprising an amino acid

25 of residues 16 through 323 of Figure 116 (SEQ ID NO:210). sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence In a further aspect, the invention concerns an isolated PRO1298 polypeptide, comprising an amino acid

30 of amino acid residues 16 to about 323, inclusive of Figure 116 (SEQ ID NO:210), or a fragment thereof a qualitative biological activity of a native PRO1298 polypeptide. sufficient to provide a binding site for an anti-PRO1298 antibody. Preferably, the PRO1298 fragment retains In yet another aspect, the invention concerns an isolated PRO1298 polypeptide, comprising the sequence

ઝ sequence of amino acid residues from about 16 to about 323, inclusive of Figure 116 (SEQ 1D NO:210), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence molecule under stringent conditions with (a) a DNA molecule encoding a PRO1298 polypeptide having the identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the pulypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1298 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1298 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a native PRO1298 polypeptide, by contacting the native PRO1298 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO 1298 polypeptide, or an agonist or amagonist as hereinabove defined, in combination with a pharmaceutically acceptable currier.

59. PRO130

A cDNA clone (DNA66512-1564) has been identified that encodes a novel polypeptide having bomology to cytochrome P450 and designated in the present application as "PRO1301."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO 1301 polypeptide.

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In one aspect, the isolated mucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1301 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 462, inclusive of Figure 118 (SEQID NO:212), or (b) the complement of the DNA molecule of (a).

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In another sepect, the invention concerns an isolated nucleic acid molecule encoding a PRO1301 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 97 and about 1428, inclusive, of Figure 117 (SEQ ID NO:211). Preferably, bybridization occurs under stringent hybridization and wash conditions.

25 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA is ATCC Deposit No. 203218 (DNA66512-1564), or (b) the complement of the DNA molecule of (a). In a preferred embediation, the nucleic 30 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203218 (DNA66512-1564).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 462, inclusive of Figure 118 (SEQ ID NO:212), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

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nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1301 polypeptide having the sequence of amino acid residues from about 19 to about 462, inclusive of Figure 118 (SEQ ID NO:212), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1301 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 18 in the sequence of Figure 118 (SEQ ID NO:212). The transmembrane domain has been tentatively identified as extending from about amino acid position 271 through about amino acid sequence (Figure 118, SEQ ID NO:212).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more 15 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the armino acid sequence of residues 19 to about 462, inclusive of Figure 118 (SEQ ID NO:212), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1301 polypeptide roding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, 20 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and must preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1301 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

25 embodiment, includes an amino acid sequence comprising residues 19 to 462 of Figure 118 (SEQ ID NO.212), In associate aspect, the invention provides in subased PRO1301 polypeptide, comprising an amino acid sequence occurrent an isolated PRO1301 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 452, inclusive of Figure 118 (SEQ ID NO.212).

In a further aspect, the invention concerns an isolated PRO1301 polypeptide, comprising an amino acid sequence acording at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 19 to 462 of Figure 118 (SEQ ID NO:212).

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In yet another aspect, the invention concerns an isolated PRO1301 polypeptide, comprising the sequence 35 of amino acid residues 19 to about 462, inclusive of Figure 118 (SEQ ID NO:212), or a fragment thereof sufficient to provide a binding site for an anti-PRO1301 antibody. Preferably, the PRO1301 fragment retains a qualitative biological activity of a native PRO1301 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1301 polypeptide having the sequence of amino acid residues from about 19 to about 462, inclusive of Figure 118 (SEQ ID NO:212), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about a 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity (i) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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60. PRO1268

10 A cDNA clone (DNA66519-1535) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1268."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1188 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

15 preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity most

preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1268 polypeptide having

the sequence of amino acid residues from about 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214), or

(b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated metric acid molecule encoting a PRO1268
20 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 89 and about 508, inclusive, of Figure 119 (SEQ ID NO:213). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having
at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least
25 about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule
encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203236
(DNA66519-1335), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic
acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
Deposit No. 203236 (DNA66519-1335).

30 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 mucleotides, and preferably at least about 100 mucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1268 polypeptide having the sequence of

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amino acid residues from about 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity in (a) or (b), including the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1268 polypeptide, with one or more of its soluble, i.e. transmembrane, domains deleted or inactivated or is complementary to such encoding nucleic acid molecule. Transmembrane domains has been tentatively identified at about amino acids 12-28 (type II), 51-66, and 107-124 in the PRO1268 amino acid sequence (Figure 120, SEQ ID NO.214).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA 10 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1268 polypeptide coding sequence that may find
15 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotidas in length,
preferably from about 20 to about 60 nucleotidas in length, more preferably from about 20 to about 50 nucleotidas in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1268 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

20 In a specific aspect, the invention provides isolated native sequence PRO1268 polypeptide, which in one embodiment, includes an amino acid requence comprising residues 1 to 140 of Figure 120 (SEQ ID NO.214).

In another aspect, the invention concerns an isolated PRO1268 polypeptide, comprising an amino acid sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity.

In a further aspect, the invention concerns an isolated PRO1268 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 80% positives, most preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 140 of Figure 120 (SEQ ID NO:214).

In yet another aspect, the invention concerns an isolated PRO1268 polypeptide, comprising the sequence of amino acid residues 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214), or a fragment thereof sufficient to provide a binding site for an anti-PRO1268 antibody. Preferably, the PRO1268 fragment retains a qualitative biological activity of a native PRO1268 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a tent DNA 35 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1268 polypeptide having the sequence of amino acid residues from about 1 to about 140, inclusive of Figure 120 (SEQ ID NO:214), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence

identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

61. PRO1269

A cDNA clone (DNA66520-1536) has been identified that encodes a novel polypeptide having homology to granulocyte peptide A and designated in the present application as "PRO1269."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding 01269 polypeptide.

- 10 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1269 polypoptide having the sequence of amino acid residues from 1 or about 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216), or (b) the complement of the DNA molecule of (a).
- In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1269
 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 86 and
 about 613, inclusive, of Figure 121 (SEQ ID NO:215). Preferably, hybridization occurs under stringent
 hybridization and wash conditions.
- In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity to (a) a DNA molecule encoding the same mature polypepidie encoded by the human protein cDNA in ATCC Deposit No. 203226 (DNA66520-1536), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic scrid comprises a DNA encoding the same mature polypepide encoded by the human protein cDNA in ATCC Deposit No. 203226 (DNA66520-1536).

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to a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA emooding a polypepide having at least about 80% sequence identity, proferably at least about 85% sequence identity, more preferably at least about 90% sequence identity. most preferably at least about 95% acquence identity to the sequence of amino acid residues from about 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and profuced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1269 polypeptide having the acquence of amino acid residues from about 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about at 80% acquence identity, preferably at least about at 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1269 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 20 in the sequence of Figure 122 (SEQ ID NO:216).

- In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to about 196, inclusive of Figure 122 (SEQ ID NO:21)6, or (b) the complement of the DNA of (a).
- Another embodiment is directed to fragments of a PRO1259 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1269 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

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In a specific aspect, the invention provides itolated native sequence PRO1269 polypopide, which in one embodiment, includes an amino acid sequence comprising residues 21 to 196 of Figure 122 (SEQ ID NO.216). In another aspect, the invention concerns an itolated PRO1269 polypopide, comprising an amino acid

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more 20 preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216).

In a further aspect, the invention concerns an isolated PRO 1269 polypoptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence 25 of residues 21 to 196 of Figure 122 (SEQ ID NO:216).

In yet snother aspect, the invention concerns an isolated PRO1269 polypeptide, comprising the sequence of amino acid residues 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216), or a fragment thereof sufficient to provide a binding site for an anti-PRO1269 antibody. Preferably, the PRO1269 fragment retains a qualitative biological activity of a native PRO1269 polypeptide.

30 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1269 polypeptide having the sequence of amino acid residues from about 21 to about 196, inclusive of Figure 122 (SEQ ID NO:216), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agenists and antagonists of a native PRO1269 polypeptide. In a particular embodiment, the agenist or antagonist is an anti-PRO1269 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1269 polypeptide, by contacting the native PRO1269 polypeptide with a candidate molecule and rounitoring a biological activity mediated by said polypeptide.

In a still further embodiment. the invention concerns a composition comprising a PRO 1269 polypeptide or an agmist or amagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

62. PRO132

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A cDNA close (DNA66521-1583) has been identified, having homology to nucleic acid encoding perurexopilin, that encodes a novel polypeptide, designated in the present application as "PRO1327".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1327 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1327 polypeptide having the sequence of amino acid retidues from about 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO:218), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1327 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleoxides 55 or about 97 and about 810, inclusive, of Figure 123 (SEQ ID NO:217). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 80% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypoptide encoded by the human protein cDNA in ATCC Deposit No. 203225 (DNA66521-1583) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypoptide encoded by the human protein cDNA in ATCC Deposit No. 203225 (DNA66521-1583).

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In still a further aspect, the invention concerns an isolated model: acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO:218), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 260 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1327 polypeptide having the sequence of amino acid residues from 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO:218), or (b) the complement of the DNA molecule of (a), and,

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if the DNA molecule has at least about an 80% sequence identity, prefereably at least about on 85% sequence identity, more preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (4) or (h), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1327 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been transitively identified as extending from about amino acid position I to about amino acid position 14 in the sequence of Figure 124 (SEQ ID NO:218).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more 10 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO:218), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1327 polypeptide coding sequence that may find use as bybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,

15 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 123 (SEQ ID NO:217).

In another embodiment, the invention provides isolated PRO 1327 polypeptide encoded by any of the isolated multic acid sequences bereinabove identified.

20 In a specific aspect, the invention provides isolated native sequence PRO1327 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 15 to about 252 of Figure , 124 (SEQ ID NO:218).

In mother aspect, the invention concerns an isolated PRO1327 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO:218).

In a further aspect, the invention concerns an isolated PRO1327 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence 30 of residues 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID NO.218).

In yet another aspect, the invention concerns an isolated PRO1327 polypepide, comprising the sequence of amino acid residues 1 or about 15 to about 252, inclusive of Figure 124 (SEQ 1D NO:218), or a fragment thereof sufficient to provide a binding site for an anti-PRO1327 antibody. Preferably, the PRO1327 fragment returns a qualitative biological activity of a mative PRO1327 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1227 polypeptide having the requence of amino acid residues from about 1 or about 15 to about 252, inclusive of Figure 124 (SEQ ID

NO.218), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about an 95% sequence identity to (a) or (b), (ii) culturing a host oell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agazists and antagonists of a native PRO1327 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1327 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1327 polypeptide by contacting the native PRO1327 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO 11377 polypeptide, or an agonist or antagunist as hereinabove defined, in combination with a pharmaceutically acceptable carrier,

63. PRO138

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A cDNA clone (DNA66526-1616) has been identified that encodes a rovel polypeptide having homology to exrebellin and designated in the present application as "PRO[382."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1382 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1382 polypeptide having the sequence of amino acid residues from 1 or about 28 to about 201, inclusive of Figure 126 (SEQ ID NO:220), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1382 polypepuide comprising DNA hybridizing to the complement of the nucleic acid between about residues 418 and about 939, inclusive, of Figure 125 (SEQ ID NO:219). Proferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule cucoding the same mature polypeptide excoded by the human protein cDNA in ATCC Deposit No. 202246 (DNA66526-1616), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC

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In a still further aspect, the invention concerns an Isolated nucleic soid molecule comprising (a) DNA encoding a polypoptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to the sequence of amino acid residues from about 28 to about 201, inclusive of Figure 126 (SEQ ID identity to the sequence of amino acid residues from about 28 to about 201, inclusive of Figure 126 (SEQ ID

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Deposit No. 203246 (DNA66526-1616).

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NO:220), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleoic acid molecule having at least about 30 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1382 polypeptide having the sequence of animo acid residues from about 28 to about 201, inclusive of Figure 126 (SEQ ID NO.220), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

a PRO 1382 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding nucleic said molecule. The signal peptide has been tentatively identified as extending from unino acid position I through about amino acid position 27 in the sequence of Figure 126 (SEQ ID NO.220).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 90% positives, more preferably at least about 90% positives when compared with the amino acid sequence of residues 28 to about 201, inclusive of Figure 126 (SEQ ID NO:220), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1382 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1382 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1382 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 28 to 201 of Figure 126 (SEQ ID NO:220).

In another aspect, the invention concerns an isolated PRO1382 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 28 to about 201, inclusive of Figure 126 (SEQ ID NO:220).

In a further aspect, the invention concerns an isolated PRO 1382 polypeptide, comprising an amino acid 30 sequence sooring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 28 to 201 of Figure 126 (SEQ ID NO:220).

In yet another aspect, the invention concerns an ioniand PRO1382 polypeptide, comprising the sequence of amino acid residues 28 to about 201, inclusive of Figure 126 (SEQ ID NO.220), or a fragment thereof 35 sufficient to provide a binding site for an anti-PRO1382 amthody. Preferably, the PRO1382 fragment retains a qualizative biological activity of a native PRO1382 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture. identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence sequence of amino acid residues from about 28 to about 201, inclusive of Figure 126 (SEQ ID NO:220), or (b) molecule under stringent conditions with (a) a DNA molecule encoding a PRO1382 polypeptide having th

polypeptide. In a particular embodiment, the agonist or amagonist is an anti-PRO1382 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1382

native PRO1382 polypeptide, by contacting the native PRO1382 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide. In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

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or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO 1382 polypeptide,

2 PRO1328

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designated in the present application as "PRO1328". A cDNA clone (DNA66658-1584) has been identified that encodes a novel transmembrane polypeptide,

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

- 20 the sequence of amino acid residues from about 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO 1328 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most NO:225), or (b) the complement of the DNA molecule of (a). In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,
- 25 about 66 and about 779, inclusive, of Figure 127 (SEQ ID NO:224). Preferably, hybridization occurs under polypeptide comprising DNA hybridizing to the complement of the nucleic acid between abour nucleotides 9 or stringent hybridization and wash conditions. In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1328
- 35 엉 nt least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least ATCC Deposit No. 203229 (DNA66658-1584). (DNA66658-1584) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203229 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence

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NO:225), or (b) the complement of the DNA of (a). identity to the sequence of amino acid residues I or about 20 to about 257, inclusive of Figure 128 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence

if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence about 257, inclusive of Figure 128 (SEQ ID NO:225), or (b) the complement of the DNA molecule of (s), and molecule encoding a PRO1328 polypeptide having the sequence of amino acid residues from 1 or about 20 to nucleoides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 475

- 5 domains have been tentatively identified as extending from about amino acid position 32 to about amino acid its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding a PRO1328 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and position 1 to about amino acid position 19 in the sequence of Figure 128 (SEQ ID NO:225). The transmembrane nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding
- ᅜ position 235 in the PRO1328 amino acid sequence (Figure 128, SEQ ID NO:225). position 152 to about amino acid position 169 and from about arrino acid position 216 to about amino acid position 51, from about amino acid position 119 to about amino acid position 138, from about amino acid
- 20 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more the complement of the DNA of (a). amino acid sequence of residues 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID NO:225), or (b) preferably at least about 90% positives, most preferably at least about 95% positives when compared with the In another aspect, the invention concerns an isolated nucleic acid molecule comprising. (a) DNA
- 23 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 from the nucleotide sequence shown in Figure 127 (SEQ ID NO:224). oucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived Another embodiment is directed to fragments of a PRO1328 polypeptide coding sequence that may find
- ઝ isolated nucleic acid sequences hereinabove identified. In another embodiment, the Invention provides isolated PRO1328 polypeptide encoded by any of the
- certain embodiments, includes an amino acid sequence comprising residues 1 or about 20 to about 257 of Figure 128 (SEQ 1D NO:225). tn a specific aspect, the invention provides isolated native sequence PRO1328 polypeptide, which in
- 35 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID NO:225) In another aspect, the invention concerns an isolated PRO1328 polypeptide, comprising an amino acid

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of residues 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID NO:225). about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated PRO1328 polypeptide, comprising an amino actor

of amino acid residues 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID NO:225), or a fragment thereof sufficient to provide a binding site for an anti-PRO1328 antibody. Preferably, the PRO1328 fragment retains a qualitative biological activity of a native PRO1328 polypepside. In yet another aspect, the invention concerns an isolated PRO1328 polypeptide, comprising the sequence

5 recovering the polypeptide from the cell culture. sequence of amino acid residues from about 1 or about 20 to about 257, inclusive of Figure 128 (SEQ ID cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a NO:225), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about molecule under stringent conditions with (a) a DNA molecule encoding a PRO1328 polypeptide having the In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

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designated in the present application as "PRO1325". A cDNA clone (DNA66659-1593) has been identified that encodes a novel transmembrane polypeptide.

a PRO1325 polypeptide. In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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the sequence of amino acid residues from about 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227), or (b) the complement of the DNA molecule of (a). preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO 1325 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity.

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under stringent hybridization and wash conditions. or about 105 and about 2546, inclusive, of Figure 129 (SEQ ID NO:226). Preferably, hybridization occurs polyperaide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 51 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1325

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nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in (DNA66659-1593) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least ATCC Deposit No. 203269 (DNA66659-1593). about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203269 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

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identity to the sequence of amino acid residues 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence NO:227), or (b) the complement of the DNA of (a). encoding a polypepside having at least about 80% sequence identity, preferably at least about 85% sequence In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DN/

if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence about 832, inclusive of Figure 130 (SEQ ID NO:227), or (b) the complement of the DNA molecule of (a), and nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1325 polypeptide having the sequence of amino acid residues from 1 or about 19 to In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100

identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

20 15 627 and from about amino acid position 751 to about amino acid position 770 in the PRO1325 amino acid nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid sequence (Figure 130, SEQ ID NO:227). position 501 to about amino acid position 520, from about amino acid position 607 to about amino acid position position 317, from about amino acid position 451 to about amino acid position 470, from about amino acid its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding a PRO1325 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and domains have been tentatively identified as extending from about amino acid position 292 to about amino acid position 1 to about amino acid position 18 in the sequence of Figure 130 (SEQ ID NO:227). The transmembrane

23 amino acid sequence of residues 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227), or (b) the complement of the DNA of (a). preferably at least about 90% positives, most preferably at least about 95% positives when compared with the encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

preferably from about 20 to about 60 nucleorides in length, more preferably from about 20 to about 50 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, Another embodiment is directed to fragments of a PRO1325 polypeptide coding sequence that may find

8 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 129 (SEQ ID NO:226). In another embodiment, the invention provides isolated PRO1325 polypeptide encoded by any of the

35 In a specific aspect, the invention provides isolated native sequence PRO1325 polypeptide, which in

isolated nucleic acid sequences hereinabove identified.

certain embodiments, includes an amino acid sequence comprising residues 1 or about 19 to about 832 of Figure 130 (SEQ ID NO:227).

In another aspect, the invention concerns an isolated PRO1325 polypeptide, comprising an amino acid

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to the preferably at least about 90% sequence identity to the sequence of amino acid residues 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227).

In a further aspect, the invention concerns an isolated PRO 1325 polypeptide, comprising an amino acid sequence ecoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227).

In yet another aspect, the invention concerns an isolated PRO1325 polypeptide, comprising the sequence of amino acid residues 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO:227), or a fragment thereof sufficient to provide a binding site for an anti-PRO1325 antibody. Preferably, the PRO1325 fragment retains a qualitative biological activity of a native PRO1325 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1325 polypeptide having the sequence of amino acid residues from about 1 or about 19 to about 832, inclusive of Figure 130 (SEQ ID NO-227), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b). (ii) culturing a best cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

20 66. PRO1340

A cDNA clone (DNA66663-1598) has been identified that encodes a novel polypeptide having homology to Ksp-cadherin and designated in the present application as *PRO1340.*

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1340 polyperaide.

- In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to (a) a DNA molecule encoding a PRO1340 polypoptide having the sequence of amino acid residues from 1 or about 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229), or (b) the complement of the DNA molecule of (a).
- 30 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1340 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 182 and about 2548, inclusive, of Figure 131 (SEQ ID NO:228), Preferably, hybridization occurs under stringent hybridization and wash conditions.
- In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having
 35 at least about 80% acquence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule
 encoding the same mature polypeptide encoded by the human protein eDNA in ATCC Deposit No. 203268

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(DNA66663-1598), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203268 (DNA66663-1598).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% requence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229), or the complement of the DNA of (a).

In a further aspect, the invention concurs an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule 100 under stringent conditions with (a) a DNA molecule encoding a PRO1340 polypeptide having the sequence of amino with residues from about 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229), or (h) the complement of the DNA molecule of (a), and, If the DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity in (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1340 polypeptide, with or without the N-terminal signal sequence analor the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or it complementary to such encoding nucleic acid molecule. The signal peptide has been tensatively identified as extending from amino acid position 18 in the sequence of Figure 132 (SEQ ID NO:229). The transmembrane domain has been tensatively identified as extending from about amino acid position 762 to about amino acid omnin has been tensatively identified as extending from about amino acid position 762 to about amino acid

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 83% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the

position 784 in the PRO1340 amino acid sequence (Figure 132, SEQ ID NO:229).

25 amino acid sequence of residues 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229), or (h) the complement of the DNA of (a).
Another embodiment is directed to fragments of a PRO1340 polypoptide coding sequence that may find

use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1340 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1340 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 19 to 807 of Figure 132 (SEQ ID NO.229).

In another aspect, the invention concerns an isolated PRO1340 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to the

sequence of amino acid residues 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229).

In a further aspect, the invention concerns an isolated PRO 1340 polypopide, comprising an amino acid sequence scoring at least about 89% positives, preferably at least about 89% positives, more preferably at least about 99% positives, more preferably at least about 99% positives when compared with the amino acid sequence of residues 19 to 807 of Figure 132 (SEQ ID NO:229).

In yet another aspect, the invention concerns an isolated PRO1340 polypeptide, comprising the sequence of amino acid residues 19 to about 807, inclusive of Figure 132 (SEQ ID NO:229), or a fragment thereof sufficient to provide a binding site for an anti-PRO1340 antibody. Preferably, the PRO1340 fragment retains a qualitative biological activity of a native PRO1340 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA nolecule encoding a PRO1340 polypeptide having the sequence of amino acid residues from about 19 to about 807, inclusive of Figure 132 (SEQ ID NO.229), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns againsts and antagonists of a native PRO1340 polypropide. In a particular embodiment, the agonist or antagonist is an anti-PRO1340 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1340 polypeptide, by contacting the native PRO1340 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO1340 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

67. PRO1339

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A cDNA clone (DNA66669-1597) has been identified that encodes a novel pollypeptide having sequence identity with carboxypeptidases and designated in the present application as "PRO1339."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1339 polypeptide.

30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1339 polypoptide having the sequence of amino acid residues from 1 or about 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234), or (b) the complement of the DNA molecule of (a).

35 In another aspect, the invention concerns an isolated nucleit: acid molecule encoding a PRO1339 polypeptide comprising DNA bybridizing to the complement of the nucleic acid between about residues 58 and about 1271, inclusive, of Figure 133 (SEQ ID NO:233). Preferably, bybridization occurs under stringent

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hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity to (a) a DNA molecule shout 90% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203272 5 (DNA66669-1597), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of antiso acid residues from about 17 to about 421, inclusive of Figure 124 (SEQ ID NO:234), or the complement of the DNA of (a).

Deposit No. 203272 (DNA66669-1597).

soid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 anucleoides, and preferably at least about 100 nucleoides and produced by hybridizing a test DNA molecule 15 under stringent conditions with (a) a DNA molecule encoding a PRO1339 polypeptide having the sequence of amino acid residues from about 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

20 In another aspect, the invention concerns an isolated nucleic axid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino axid tequence of residues 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1339 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1339 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

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In a specific aspect, the invention provides isolated native sequence PRO1339 polypoptide, which in one embodiment, includes an amino acid sequence comprising residues 17 through 421 of Figure 134 (SEQ II) NO:234).

In another expect, the invention concerns an isolated PRO1339 polypeptide, comprising an amino acid

35 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more
preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
sequence of amino acid residues 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234).

In a further aspect, the invention concerns an isolated PRO1339 polypeptide, comprising an amino acid sequence exoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 17 through 421 of Figure 134 (SBQ ID NO:234).

In yet another aspect, the invention concerns an isolated PRO1339 polypeptide, comprising the sequence of amino acid residues 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234), or a fragment thereof sufficient to provide a binding site for an anti-PRO1339 antibody. Preferably, the PRO1339 fragment retains a qualitative biological activity of a native PRO1339 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1339 polypeptide having the sequence of amino acid residues from about 17 to about 421, inclusive of Figure 134 (SEQ ID NO:234), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity of (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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In yet another embodinent, the invention concerns agentists and antagonists of a native PRO1339 polypeptide. In a particular embodinent, the agentist or antagonist is an anti-PRO1339 antibody.

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In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a native PRO1339 polypeptide, by contacting the native PRO1339 polypeptide with a cambidate molecule and monitoring a binlogical activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO 1339 polypeptide, or an agenist or an agenist or an agenist or an agenist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

68. PROIS

25 A cDNA clone (DNA66672-1586) has been identified that encodes a novel polypeptide having homology to human thyroxine-binding globulin designated in the present application as *PRO1337*.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1337 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

30 preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most
preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1337 polypeptide having
the sequence of saniso acid residues from 1 or about 21 to about 417, Inclusive of Figure 136 (SEQ ID NO:236),
or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1337

35 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 120 and about 1310, inclusive, of Figure 135 (SEQ ID NO:235). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203265 (DNA66672), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203265 (DNA66672-66672).

10 identity to the sequence of amino acid residues from about 21 to about 417, inclusive of Figure 136 (SEQ ID NO:226), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1337 polypeptide having the sequence of amino acid residues from about 21 to about 417, inclusive of Figure 136 (SEQ ID NO.236), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about a 90% sequence identity, preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an Isolated nucleic acid molecule comprising DNA encoding 20 a PRO1337 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionize, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 20 in the sequence of Figure 136 (SEQ ID NO:236).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
25 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
armino acid sequence of residues 21 to about 417, inclusive of Figure 136 (SEQ ID NO:236), or (b) the
complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1337 polypeptide coding sequence that may find 30 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embediment, the invention provides isolated PRO1337 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

35 In a specific aspect, the invention provides isolated native sequence PRO 1337 polypoptide, which in one embodiment, includes an amino acid sequence comprising residues 21 to 417 of Figure 136 (SEQ ID NO:236). In another aspect, the invention concerns an isolated PRO 1337 polypoptide, comprising an amino acid

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of artino acid residues 21 to about 417, inclusive of Figure 136 (SEQ ID NO:236).

In a further espect, the invention concerns an isolated PRO1337 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 85% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to 417 of Figure 136 (SEQ ID NO:236).

In yet another aspect, the invention concerns an isolated PRO1337 polypeptide, comprising the sequence of amino acid residues 21 to about 417, inclusive of Figure 136 (SEQ ID NO:236), or a fragment thereof sufficient to provide a binding site for an anti-PRO1337 antibody. Preferably, the PRO1337 fragment retains a qualitative biological activity of a native PRO1337 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1337 polypeptide having the sequence of amino acid residues from about 21 to about 417, inclusive of Figure 126 (SEQ ID NO.236), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about a 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 95% sequence identity, or (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1337-20 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1337 antibody.

In a further embodiment, the invention concerns a method of Identifying agoalists or antagonists of a native PRO1337 polypeptide, by contacting the native PRO1337 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO 1337 polypeptide or an agonist or an agonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

y. PKOLSAZ

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A cDNA clone (DNA66674-1599) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1342".

In one embroliment the invention months as included and include the content of the

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO 1342 polypeptide.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1342 polypoptide having the sequence of amino soid residues from 1 or about 21 to about 596, inclusive of Figure 138 (SEQ ID NO:243), or (b) the complement of the DNA molecule of (a).

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in another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1342

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polypoptide comprising DNA hybridizing to the complement of the nucleic used between about residues 299 and about 2026, inclusive, of Figure 137 (SEQ ID NO:242). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity in (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203281 (DNA66674-1599), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203281 (DNA66674-1599).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 21 to about 596, inclusive of Figure 138 (SEQ ID NO:243), or the complement of the DNA of (a).

15 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1342 polypeptide having the sequence of summo acid residues from about 21 to about 596, inclusive of Figure 138 (SEQ ID NO.243), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity in the 100 or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1342 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble variants (i.e. transmembrane domain deleted or inactivated), or is complementary to such encoding the solid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 20 in the sequence of Figure 138 (SEQ ID NO:243). The transmembrane domain has been tentatively identified as extending from about amino acid position 510 to about amino acid position 532 in the PRO1342 amino acid sequence (Figure 138, SEQ ID NO:243).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

30 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives; more
preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
amino acid sequence of residues 21 to about 596, inclusive of Figure 138 (SEQ ID NO:243), or (b) the
complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1342 polypeptide coding sequence that may find 35 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more by the state of the state o

In another embodiment, the invention provides isolated PRO1342 polypeptide encoded by any of the isolated sucteic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1342 polypeptide, which in one embodimem, includes an amino acid sequence comprising residues 21 to 596 of Figure 138 (SEQ ID NO:243).

In another aspect, the invention concerns an isolated PRO1342 polypoptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 21 to about 59%, inclusive of Figure 138 (SEQ ID NO:243).

In a further aspect, the invention concerns an isolated PRO1342 polypeptide, comprising an amino acid sequence ecoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to 596 of Figure 138 (SEQ ID NO:243).

In yet mother aspect, the invention concerns an itolated PRO1342 polypeptide, comprising the sequence of amino acid residues 21 to about 596, inclusive of Figure 138 (SEQ ID NO.243), or a fragment thereof sufficient to provide a binding site for an anti-PRO1342 antibody. Preferably, the PRO1342 fragment retains a qualitative biological activity of a native PRO1342 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1342 polypeptide having the sequence of amino acid residues from about 21 to about 596, inclusive of Figure 138 (SEQ ID NO:243), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity to (a) or (b), (ii) culturing a bost cell comprising

the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the

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25 70. PRO1343

polypeptide from the cell culture

A cDNA clone (DNA66675-1587) has been identified that encodes a novel secreted polypeptide, designated in the present application as "PRO1343".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1343 polypeptide.

- 30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1343 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248), or (b) the complement of the DNA molecule of (a).
- In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1343 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 71 or about 146 and about 811, inclusive, of Figure 139 (SEQ ID NO:247). Preferably, hybridization occurs under

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stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated modelic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity in (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein eDNA in ATCC Deposit No. 203282 (DNA66675-1587) or (b) the complement of the murleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203282 (DNA66675-1587).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA 15 molecule euroding a PRO1343 polypeptide having the sequence of amino acid residues from 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferrably at least about an 80 % sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity of (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1343 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentuitedy identified as extending from about amino acid position 15 in the sequence of Figure 140 (SEQ ID NO:248).

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- 25 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA emocding a polypeptide storing at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248), or (b) the complement of the DNA of (a).
- Another embodiment is directed to fragments of a PRO1343 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 mecleotides in length, preferably from about 20 to about 60 mecleotides in length, more preferably from about 20 to about 50 mecleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 139 (SEQ ID NO.247).
- 35 la another embodiment, the invention provides tsolated PRO1343 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1343 polypeptide, which in

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certain embodiments, includes an amino acid sequence comprising residues I or about 26 to about 247 of Figure 140 (SEQ ID NO:248).

In another aspect, the invention concerns an isolated PRO1343 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248).

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In a further stycer, the invention concerns an isolated PRO1343 polypoptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248).

10 In yet another aspect, the invention concerns an isolated PRO1343 polypoptide, comprising the sequence of amino acid residues 1 or about 26 to about 247, inclusive of Figure 140 (SEQ ID NO:248), or a fragment thereof sufficient to provide a binding site for an anti-PRO1343 antibody. Preferably, the PRO1343 fragment retains a qualitative biological activity of a native PRO1343 polypoptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA IS molecule under stringent conditions with (a) a DNA molecule encoding a PRO1343 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 247, Inclusive of Figure 140 (SEQ ID NO:248), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, incut preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

71. PRO1480

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A cDNA clone (DNA67962-1649) has been identified that encodes a novel polypeptide having homology to Semaphorin C and designated in the present application as "PRO1480;"

In one embodinear, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO 1480 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1480 polypeptide having the sequence of amino acid residues from about 1 to about 837, inclusive of Figure 142 (SEQ ID NO:253), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1480 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 241 and about 2751, inclusive, of Figure 141 (SEQ ID NO:252). Preferably, hybridization occurs under stringent bybridization and wash conditions.

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in a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

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at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule effecting the same manuse polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203291 (DNA67962-1649), or (h) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same manuse polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203291 (DNA67962-1649).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA cnooding a polypeptide having at least about 85% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 837, inclusive of Figure 142 (SEQ ID NO:253), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1480 polypspide having the acquence of amino acid residues from about 1 to about 837, inclusive of Figure 142 (SEQ ID NO.253), or (b) the 15 complement of the DNA molecule of (a), and, if the DNA molecule has at least about at 90% sequence identity, preferably at least about at 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1490 polypopide, its soluble variants, (i.e. transmembrane domains deleted or inactivated) or is complementary to such encoding nucleic acid molecule. Transmembrane domains have been tentatively identified as extending from about amino acid position 23 to about amino acid position 46 (type II) and about amino acid position 718 to about amino acid position 738 in the PRO1480 amino acid sequence (Figure 142, SEQ ID NO:233).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

25 cacoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
amino acid sequence of residues 1 to about 837, inclusive of Figure 142 (SEQ ID NO:253), or (b) the
complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1480 polypeptide coding sequence that may find 30 use as hybridization probes. Such medicic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1480 polypoptide encoded by any of the isolated nucleic usid sequences hereinshove defined.

35 In a specific aspect, the invention provides todated native requence PRO1480 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 837 of Figure 142 (SEQ ID NO:253). In another aspect, the invention concerns an isolated PRO1480 polypeptide, comprising an amino acid

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to the preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 837, inclusive of Figure 142 (SEQ ID NO:253).

In a further aspect, the invention concerns an isolated PRO [480 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, most preferably at least about 95% positives when compared with the amino acid requence of residues 1 to 837 of Figure 142 (SEQ ID NO:253).

In yet another aspect, the invention concerns an isolated PRO1480 polypeptide, comprising the sequence of amino acid residues 1 to about 837, inclusive of Figure 142 (SEQ ID NO.253), or a fragment thereof sufficient to provide a binding site for an anti-PRO1480 antibody. Preferably, the PRO1480 fragment retains a qualitative biological activity of a native PRO1480 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule emoding a PRO1480 polypeptide having the sequence of amino acid residues from about 1 to about 837, inclusive of Figure 142 (SEQ ID NO.253), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at tests about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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In yet another embodiment, the invention concerns agonists and antagorists of a native PRO1480 20 polypeptide. In a particular embodiment, the agonist or antagonist is an ami-PRO1480 antibody.

In a further embodiment, the invention concerns a method of identifying agentiss or assagonists of a maive PRO1480 polypeptide, by contacting the native PRO1480 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO 1480 polypeptide, or an agonist or antagonist as hereimabove defined, in combination with a pharmaceutically acceptable carrier.

72. PRO1487

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A cDNA close (DNA68836-1656) has been identified that encodes a novel polypeptide having homology to fringe protein and designated in the present application as *PRO1487".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1487 polypeptide.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1487 polypepide having the sequence of amino acid residues from 1 or about 24 to about 802, inclusive of Figure 144 (SEQ ID NO:260), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1487

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polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 558 and about 2894, inclusive, of Figures 143A-8 (SEQ ID NO:259). Preferably, hybridization occurs under stringent bybridization and wash conditions.

It a further espect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203455 (DNA68836-1656), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203455 (DNA68836-1656).

10 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 24 to about 802, inclusive of Figure 144 (SEQ ID NO:250), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated mucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1487 polypeptide having the sequence of amino acid residues from about 24 to about 802, inclusive of Figure 144 (SEQ ID NO:260), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about at 80% sequence identity, more preferably at least about at 90% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1487 polypeptide, with or without the N-terminal signal sequence and/or the initiating, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position I through about amino acid position 23 in the sequence of Figure 144 (SEQ ID NO:260).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the 30 amino acid sequence of residues 24 to about 80%, inclusive of Figure 144 (SEQ ID NO:260), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO 1487 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1487 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

embodiment, includes an amino acid sequence comprising residues 24 to 802 of Figure 144 (SEQ ID NO:260). In a specific aspect, the invention provides isolated thative sequence PRO1487 polypeptide, which in one

sequence of amino acid residues 24 to about 802, inclusive of Figure 144 (SEQ ID NO:260). preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more In another aspect, the invention concerns an isolated PRO1487 polypeptide, comprising an amino acid

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of residues 24 to 802 of Figure 144 (SEQ ID NO:260). about 90 % positives, most preferably at least about 95 % positives when compared with the amino acid sequence sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated PRO1487 polypeptide, comprising an amino acid

5 of amino acid residues 24 to about 802, inclusive of Figure 144 (SEQ ID NO:260), or a fragment thereof sufficient to provide a binding site for an anti-PRO1487 antibody. Preferably, the PRO1487 fragment retains a qualitative biological activity of a native PRO1487 polypeptide, In yet another aspect, the invention concerns an isolated PRO1487 polypeptide, comprising the sequence

20 2 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence molecule under stringent conditions with (a) a DNA molecule encoding a PRO1487 polypeptide having the polypeptide from the cell culture. identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence sequence of amino acid residues from about 24 to about 802, inclusive of Figure 144 (SEQ ID NO:260), or (b) Identity, most preferably at least about a 95% sequence identity 10 (a) or (b), (ii) culturing a bost cell comprising In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1487 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1487

native PRO1487 polypeptide, by contacting the native PRO1487 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

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or an agonist or aniagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO 1487 polypeptide.

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designated in the present application as "PRO1418." A cDNA clone (DNA68864-1629) has been identified that excedes a novel secreted polypopide

a PRO1418 polypeptide In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

š preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1418 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

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or (b) the complement of the DNA molecule of (a). the sequence of amino acid residues from 1 or about 20 to about 350, inclusive of Figure 146 (SEQ ID NO:265)

hybridization and wash conditions. about 1187, inclusive, of Figure 145 (SEQ ID NO:264). Preferably, hybridization occurs under stringent polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 195 and In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1418

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(DNA68864-1629), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least Deposit No. 203276 (DNA68864-1629). encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203276 about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

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15 identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence NO:265), or the complement of the DNA of (a). identity to the sequence of antino acid residues from about 20 to about 350, inclusive of Figure 146 (SEQ ID encoding a polypepide having at least about 80% sequence identity, proformbly at least about 85% sequence In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

20 amino seid residues from about 20 to about 350, inclusive of Figure 146 (SEQ ID NO:265), or (b) the under stringert conditions with (a) a DNA molecule encoding a PRO1418 polypeptide having the sequence of nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

23 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more complement of the DNA of (a). amino acid sequence of residues 20 to about 350, inclusive of Figure 146 (SEQ ID NO:265), or (b) the preferably at least about 90% positives, most preferably at least about 95% positives when compared with the In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

30 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleorlides in length, and most preferably from about 20 to about 40 nucleorlides in length. Another embodiment is directed to fragments of a PRO1418 polypeptide coding sequence that may find

isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated PRO1418 polypeptide encoded by any of the

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embodiment, includes an amino acid sequence comprising residues 20 through 350 of Figure 146 (SEQ ID In a specific aspect, the invention provides isolated narive sequence PRO1418 polypeptide, which in one

NO:265).

In another aspect, the invention concerns an isolated PRO1418 polypeptide, comprising an amino axid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino axid residues 20 to about 350, inclusive of Figure 146 (SEQ ID NO.265).

In a further aspect, the invention concerns an isolated PRO1418 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 20 through 350 of Figure 146 (SEQ ID NO:265).

In yet another aspect, the invention concerns an isolated PRO1418 polypepside, comprising the sequence 10 of amino acid residues 20 to about 350, inclusive of Figure 146 (SEQ ID NO:265), or a fragment thereof sufficient to provide a binding size for an anti-PRO1418 amibody. Preferably, the PRO1418 fragment retains a qualitative biological activity of a native PRO1418 polypeptide.

In a still further aspect, the invention provides a polypoptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1418 polypoptide having the 15 sequence of unino acid residues from about 20 to about 350, Inclusive of Figure 146 (SEQ ID NO:265), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about an 85% seque

in yet another embodiment, the invention concerns agonists and antagonists of a naive PRO1418 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1418 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1418 polypeptide, by contacting the native PRO1418 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO 1418 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

. PRO1472

30 A cDNA clone (DNA68866-1644) has been identified that encodes a novel polypeptide baving sequence identity with hyprophilin and designated in the present application as *PRO1472.*

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO 1472 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, as preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1472 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 466, inclusive of Figure 148 (SEQ ID NO:267).

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or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1472 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 185 and about 1531, inclusive, of Figure 147 (SEQ ID NO:266). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203283 (DNA68866-1644), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic 10 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203283 (DNA68866-1644).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA exacting a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity, more preferably at least about 95% sequence 15 identity to the sequence of amino acid residues from about 18 to about 466, inclusive of Figure 148 (SEQ ID

NO:267), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleoxides, and preferably at least about 100 nucleoxides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1472 polypeptide having the sequence of amino acid residues from about 18 to about 466, inclusive of Figure 148 (SEQ ID NO:267), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about as 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 95% sequence identity in (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA exceeding 25 a PRO1472 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domains deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position [through about amino acid position 1-17 in the sequence of Figure 148 (SEQ ID NO:267). The transmembrane domains have been tentatively identified as being from about amino acid position 131 through about amino acid position 150 and from about amino acid position 255 through about amino acid position 259 in the PRO1472 amino acid sequence (Figure 148, SEQ ID NO:267). It is understood that PRO1472 can be manipulated to contain only particular regions given the information herein, e.g. to have only the extracellular or cytoplasmic

regions only, or to have the earboxyl end truncated wherein the second transmembrane domain is deleted.

In another aspect, the invertion concerns an isolated nucleic acid molecule comprising (a) DNA

sensoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 18 to about 466, inclusive of Figure 148 (SEQ ID NO:267), or (b) the

complement of the DNA of (a).

Another embodiment is diseased to fragments of a PRO1472 polypeptide coding sequence that may find use as hybridization probes. Such nucleic seld fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length,

In another embodiment, the invention provides isolated PRO1472 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1472 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 18 through 466 of Figure 148 (SEQ ID NO:267).

10 In another aspect, the invention concerns an isolated PRO1472 polypeptide, comprising an amino acid sequence baving at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity in the sequence of amino acid residues 18 to about 466, inclusive of Figure 148 (SEQ ID NO.257).

In a further aspect, the invention concerns an isolated PRO1472 polypeptide, comprising an amino acid

5 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least
about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence
of residues 18 through 466 of Figure 148 (SEQ ID NO:267).

In yet another aspect, the invention concerns an isolated PRO1472 polypeptide, comprising the sequence of amino acid residues 18 to about 466, inclusive of Figure 148 (SEQ ID NO.267), or a fragment thereof 20 sufficient to provide a binding site for an ami-PRO1472 antibody. Preferably, the PRO1472 fragment retains a qualitative biological activity of a native PRO1472 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1472 polypeptide having the sequence of amino acid residues from about 18 to about 466, inclusive of Figure 148 (SEQ ID NO:267), or (b) 25 the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably a

30 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1472 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1472 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or anagonists of a native PRO1472 polypeptide, by contacting the native PRO1472 polypeptide with a candidate molecule and munitoring a biological activity mediated by said polypeptide.

35 In a still further embodiment, the invention concerns a composition comprising a PRO1472 polypeptide, or an agentist or antagenist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

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75. PRO1461

A cDNA close (DNA68871-1638) has been identified that eucodes a novel polypeptidehaving homology to serine protesse and designated in the present application as "PRO1461".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO 1461 polypeptide.

- In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1461 polypeptide having the sequence of amino acid residues from about 1 to about 423, inclusive of Figure 150 (SEQ ID NO:269), or (b) the complement of the DNA molecule of (a).
- 10 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1461 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 32 and about 1300, inclusive, of Figure 149 (SEO ID NO:268). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having 15 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203280 (DNA68871-88871), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203280 (DNA68871-68871)).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 1 to about 423, inclusive of Figure 150 (SEQ ID NO:259), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1461 polypoptide having the sequence of amino acid residues from about 1 to about 423, inclusive of Figure 150 (SEQ ID NO:269), or (b) the

30 complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1461 polypeptide, with or without the initiating methionine, and its soluble variants (i.e. transmembrane domain deleted or inactivated), or is complementary to such encoding nucleic acid molecule. A type II transmembrane domain has been remaitively identified as extending from about amino acid position 21 to about amino acid position 40 in the PRO1461 amino acid sequence (Figure 150, SEQ ID NO:268).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 423, inclusive of Figure 150 (SEQ ID NO:269), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1461 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length,

In another embodiment, the invention provides isolated PRO1461 polypeptide emboded by any of the isolated nucleic acid sequences hereinabove defined.

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In a specific aspect, the invention provides isolated native sequence PRO1461 polypeptide, which in one combodiment, includes an amino acid sequence comprising residues 1 to 423 of Figure 150 (SEQ ID NO:269).

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In another aspect, the invention concerns an isolated PRO1461 polypoptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 423, inclusive of Figure 150 (SEQ ID NO:269).

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In a further aspect, the invention concerns an isolated PRO1461 polypeptide, comprising an amino acid requence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 423 of Figure 150 (SEQ ID NO.269).

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In yet another aspect, the invention concerns an isolated PRO1461 polypeptide, comprising the acquence of amino acid residues 1 to about 423, inclusive of Figure 150 (SEQ ID NO:269), or a fragment thereof sufficient to provide a binding site for an amit-PRO1461 antibody. Preferably, the PRO1461 fragment retains a qualitative biological activity of a native PRO1461 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1461 polypeptide having the sequence of amino acid residues from about 1 to about 423, inclusive of Figure 150 (SEQ ID NO.269), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity to (a) or (b), (ii) culturing a bost cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1461 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1461 amthody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonias of a native PRO1461 polypeptide, by contacting the native PRO1461 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO 1461 polypeptide or an agonist or antagenist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

76. PRO1410

A cDNA clone (DNA68874-1622) has been identified that encodes a novel transmembrane polypopide designated in the present application as "PRO1410".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identify, preferably at least about 90% sequence identify; more preferably at least about 90% sequence identify to (a) a DNA molecule encoding a PRO1410 polypeptide having the sequence of amino acid residues from about 1 or about 21 to about 236, inclusive of Figure 152 (SEQ ID NO:271), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PROJ410 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 152 or about 212 and about 865, inclusive, of Figure 151 (SEQ ID NO:270). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule 20 encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 202277 (DNA68874-1622) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203277 (DNA68874-1622).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

cencoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence
identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence
identity to the sequence of amino acid residues 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID

NO:271), or (b) the complement of the DNA of (a).

In a further aspect, the invention comerns an isolated nucleic acid molecule having at least 100
30 nucleotides and produced by hybridizing a test DNA molecule under stringent coorditions with (a) a DNA
molecule encoding a PRO1410 polypeptide having the sequence of amino acid residues from 1 or about 21 to
about 238, iteclusive of Figure 152 (SEQ ID NO:271), or (b) the complement of the DNA molecule of (a), and,
if the DNA molecule has at least about an 80 % sequence identity, preferrably at least about an 85% sequence
identity, more preferably at least about a 90 % sequence identity, most preferably at least about a 95% sequence
35 identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1410 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and

its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 10 in the sequence of Figure 152 (SEQ ID NO:271). The transmembrane domain has been tentatively identified as extending from about amino acid position 194 to about amino acid position 200 in the PRO(410 amino acid sequence (Figure 152, SEQ ID NO:271).

- In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO.271), or (b) the complement of the DNA of (a).
- Another embodiment is directed to fragments of a PRO 1410 polypeptide coding sequence that may find use as hybridization probes. Such medeic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 90 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 151 (SEQ ID NO:270).
- 15 In another embodiment, the invention provides isolated PRO1410 polypeptide encoded by any of the isolated mucleic acid sequences hereinabove Identified.
- In a specific aspect, the invention provides isolated native sequence PRO1410 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 21 to about 238 of Figure 152 (SEQ ID NO:271).

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- In another aspect, the invention concerns an isolated PRO1410 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO:271).
- In a further aspect, the invention concerns an isolated PRO1410 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO:271).

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- In yet another aspect, the invention concerns an isolated PRO1410 polypeptide, comprising the sequence of amino acid residues 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO:271), or a fragment 30 thereof sufficient to provide a binding site for an anti-PRO1410 antibody. Preferably, the PRO1410 fragment retains a qualitative biological activity of a native PRO1410 polypeptide.
- In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1410 polypeptide having the sequence of amino acid residues from about 1 or about 21 to about 238, inclusive of Figure 152 (SEQ ID NO:271), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 80% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b). (ii) culturing a host

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cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1416 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1410 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1410 polypeptide by contacting the native PRO1410 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO(410 polypeptide, or an agonist or amagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

77. PRO1568

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A cUNA clone (DNA68880-1676) has been identified that encodes a novel polypeptide having sequence identity with tetraspanins and designated in the present application as *PRO1568.*

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO 1568 polypeptide.

- In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1568 polyperprior baving the sequence of emina acid residues from 1 or about 34 to about 305, inclusive of Figure 154 (SEQ ID NO:273), or (b) the complement of the DNA molecule of (a).
- 20 O In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1568 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 307 and about 1122, inclusive, of Figure 153 (SEQ ID NO:272). Preferably, hybridization occurs under stringent hybridization and wash conditions.
- In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having 25 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203319 (DNA68889-1676), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC 30 Deposit No. 203319 (DNA68889-1676).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 34 to about 305, inclusive of Figure 154 (SEQ II) NO:273), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule

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under stringent conditions with (a) a DNA molecule encoding a PRO1568 polypeptide having the sequence of arnino acid residues from about 34 to about 305, inclusive of Figure 154 (SEQ ID NO:273), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1568 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 33 in the sequence of Figure 154 (SEQ ID NO:273). The transmembrane domains have been tentatively identified as extending from about amino acids 12:35, 57-86, 94-114 and 226-248 in the PRO1568 amino acid sequence (Figure 154, SEQ ID NO:273).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 90% positives when compared with the amino acid sequence of residues 34 to about 305, inclusive of Figure 154 (SEQ ID NO:273), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1568 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1568 polypeptide encoded by any of the isolated nucleic acid sequences bereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1568 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 34 through 305 of Figure 154 (SEQ ID NO:273).

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In another aspect, the invention concerns an isolated PRO1568 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 34 to about 90%, inclusive of Figure 154 (SEQ ID NO:273).

30 In a further aspect, the invention concerns an isolated PRO1568 polypeptide, comprising an amino acid sequence scaring at least about 80% positives, preferably at least about 83% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 34 through 305 of Figure 154 (SEQ ID NO:273).

In yet another aspect, the invention concerns an isolated PRO1568 polypeptide, comprising the sequence 35 of amino acid residues 34 to about 305, inclusive of Figure 154 (SEQ ID NO:273), or a fragment thereof sufficient to provide a binding site for an anti-PRO1568 antibody. Preferably, the PRO1568 fragment retains a qualitative biological activity of a native PRO1568 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1568 polypeptide having the sequence of amino acid residues from about 34 to about 305, inclusive of Figure 154 (SEQ ID NO:273), or (b) the complement of the DNA molecule of (a), and if the less DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about an 85% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1568 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1568 antibody.

10 In a further embodiment, the invention concerns a method of identifying agorists or antagonists of a native PRO1568 polypeptide, by contacting the native PRO1568 polypeptide with a candidate molecute and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO 1568 polypoptide, or an agonist or anagonist as hereinshove defined, in combination with a pharmaceutically acceptable carrier.

78. PRO157

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A cDNA clone (DNA68885-1678) has been identified that encodes a novel polypeptide having sequence identity with SP60 and destignated in the present application as "PRO1570." In particular, for the first time. Applicants have identified an additional 199 amino acids on the amino terminal end of the protein previously identified as SP60.

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In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1570 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1570 polypeptide having the sequence of amino acid residues from about 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule emoding a PRO1570 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 210 and 30 about 1505, inclusive, of Figure 155 (SEQ ID NO:274). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule about 95% sequence identity to (b) a DNA molecule according the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203311 (DNA68885-1678), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the mucleic acid comprises a DNA encoding the same manure polypeptide encoded by the human protein cDNA in ATCC

Deposit No. 203311 (DNA68885-1678)

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to the sequence of amino acid residues from about 1 to about 432, inclusive of Figure 156 (SEQ ID NO.275), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a Lert DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1570 polypeptide having the sequence of amino acid residues from about 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. In a preferred embodiment, the probes provided herein are from the amino terminal end of the peptide identified in Figure 1, defined as amino acids 1-199 of SEQ ID NO:275.

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15 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1570 polypeptide, in a form which is secreted and is soluble, i.e. transmembrane domain deleted, truncated or inactivated variants.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more 20 preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid acquence of residues 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1570 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 merleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length. Preferably, the probes are from the amino terminal end as provided herein.

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In another embodiment, the invention provides to lated PRO1570 polypeptide encoded by any of the isolated medicic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1570 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 432 of Figure 156 (SEQ ID NO:275).

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In another aspect, the invention concerns an isolated PRO1570 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275).

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In a further aspect, the invention concerns an isolated PRO1570 polypeptide, comprising an amino acid

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sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 1 through 432 of Figure 156 (SEQ ID NO:275).

In yet another aspect, the invention concerns an isolated PRO1570 polypeptide, comprising the sequence of amino acid residues 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275), or a fragment thereof 5 sufficient to provide a binding site for an anti-PRO1570 antibody. Preferably, the PRO1570 fragment retains a qualitative bindingical activity of a native PRO1570 polypeptide.

in a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1570 polypeptide having the sequence of amino acid residues from about 1 to about 432, inclusive of Figure 156 (SEQ ID NO:275), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about m 80% sequence identity, preferably at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

15 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1570 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1570 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a maive PRO1570 polypeptide, by contacting the native PRO1570 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

20 In a still further embodiment, the invention concerns a composition comprising a PRO1570 polypeptide. or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

PRQ1317

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A cDNA clone (DNA71166-1685) has been identified that encodes a novel polypeptide having homology to semaphorin B and designated in the present application as "PRO1317".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1317 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, more preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most 30 preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1317 polypeptide having the sequence of amino acid residues from 1 or about 31 to about 761, inclusive of Figure 138 (SEQ ID NO:277), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1317 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 195 and 35 about 2387, inclusive, of Figure 157 (SEQ ID NO:276). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

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at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule about 90% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203355 (DNA71166-1685), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203355 (DNA71166-1685).

In a still further aspect, the invention concerns an isolated modelic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid restidues from about 31 to about 761, inclusive of Figure 158 (SEQ ID NO:277), or the complement of the DNA of (a).

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In a further aspece, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1317 polypeptide having the sequence of amino acid residues from about 31 to about 761, inclusive of Figure 158 (SEQ ID NO:277), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1317 polypoptide, with or without the N-terminal signal sequence and/or the initiating methionine, and 20 its soluble variants (i.e. transmembrane domains deleted or inactivated), or is complementary to such encoding muchtle acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 30 in the sequence of Figure 158 (SEQ ID NO:277). Transmembrane domains have been tentatively identified as extending from about amino acid positions 13-31, 136-156, 222-247, 474-490, and 685-704 in the PRO1317 amino acid sequence (Figure 158, SEQ ID NO:277).

In another aspect, the invention concerns an isolated modeic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 83% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to about 761, inclusive of Figure 138 (SEQ ID NO:277), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1317 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 40 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1317 polypeptide encoded by any of the isolated nucleit acid sequences hereimbove defined.

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In a specific aspect, the invention provides isolated native sequence PRO 1317 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 31 to 761 of Figure 158 (SEQ ID NO.277).

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In another aspect, the invention concerns an isolated PRO1317 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 31 to about 761, inclusive of Figure 158 (SEQ ID NO:277).

In a further aspect, the invention concerns an isolated PRO1317 polypepide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to 761 of Pigure 158 (SEQ ID NO.277).

In yet another aspect, the invention concerns an isolated PRO1317 polypeptide, comprising the sequence of amino acid residues 31 to about 761, inclusive of Figure 158 (SEQ ID NO.277), or a fragment thereof 10 sufficient to provide a binding site for an anti-PRO1317 antibody. Preferably, the PRO1317 fragment remins a qualitative biological activity of a native PRO1317 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1317 polypeptide having the sequence of amino acid residues from about 31 to about 761, inclusive of Figure 158 (SEQ 1D NO:277), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity most preferably at least about as 95% sequence identity to the control of the desired by at least about as 95% sequence.

15 the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about n 90% sequence identity, most preferably at least about as 85% sequence identity to (a) or (b), (ii) culturing a bost cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.
20 In yet another embodiment, the invention concerns againsts and anasonists of a native PRO1317

In yet another embodiment, the invention concerns againsts and anagonists of a native PRO1317 polypeptide. In a particular embodiment, the agonist or anagonist is an anti-PRO1317 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or autagonists of a native PRO1317 polypeptide, by contacting the native PRO1317 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

25 In a still further embodiment, the invention concerns a composition comprising a PRO1317 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmacentically acceptable currier

. PRO1780

A cDNA clone (DNA71169-1709) has been identified that encodes a novel polypeptide having homology 30 to glucuronosyltransferase and designated in the present application as "PRO1780".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1780 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1780 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 523, inclusive of Figure 160 (SEQ ID NO:282), or (b) the complement of the DNA molecule of (a).

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hybridization and wash conditions. about 1636, inclusive, of Figure 159 (SEQ ID NO:281). Preferably, hybridization occurs under stringent polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 125 and in another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1780

Deposit No. 203467 (DNA71169-1709). (DNA71169-1709), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA motecute encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203467 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

NO:282), or the complement of the DNA of (a). identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity to the sequence of amino acid residues from about 20 to about 523, inclusive of Figure 160 (SEQ ID In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most preferably at least residues from about 20 to about 523, inclusive of Figure 160 (SEQ ID NO:282), or (b) the complement of the conditions with (a) a DNA molecule encoding a PRO1780 polypeptide having the sequence of amino acid nucleoxides, and preferably at least about 100 and produced by hybridizing a test DNA molecule under stringent about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

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25 its soluble variants (i.e. transmembrane domain deleted or inactivated), or is complementary to such encoding position 504 in the PRO1780 amino acid sequence (Figure 160, SEQ ID NO:282). domain has been tentatively identified as extending from about amino acid position 483 to about amino acid I through about amino acid position 19 in the sequence of Figure 160 (SEQ ID NO:282). The transmembrane nucleic anid molecule. The signal peptide has been tentatively identified as extending from amino acid position a PRO1780 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

ષ્ઠ encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the complement of the DNA of (a). amino acid sequence of residues 20 to about 523, inclusive of Figure 160 (SEQ ID NO:282), or (b) the In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

33 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 Another embodiment is directed to fragments of a PRO 1780 polypeptide coding sequence that may find

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nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1780 polypeptide encoded by any of the

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more embodintem, includes an amino acid sequence comprising residues 20 to \$23 of Figure 160 (SEQ ID NO:282) In another aspect, the invention concerns an isolated PRO1780 polypeptide, comprising an amino acid In a specific aspect, the invention provides isolated native sequence PRO1780 polypeptide, which in one

preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the

10 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least of residues 20 to 523 of Figure 160 (SEQ ID NO:282). about 90% positives, most preferably at least about 95% positives when compared with the amino acid soquence sequence of amino acid residues 20 to about 523, inclusive of Figure 160 (SEQ ID NO:282). In a further aspect, the invention concerns an isolated PRO1780 polypeptide, comprising an amino acid

2 sufficient to provide a binding site for an anti-PRO1780 antibody. Preferably, the PRO1780 fragment retains of amino acid residues 20 to about 523, inclusive of Figure 160 (SEQ ID NO.282), or a fragment thereof a qualitative biological activity of a native PRO1780 polypeptide. In yet another aspect, the invention concerns an isolated PRO1780 polypeptide, comprising the sequence

molecule under stringent conditions with (a) a DNA molecule encoding a PRO1780 polypeptide having the In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

20 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence polypeptide from the cell culture. identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence sequence of amino acid residues from about 20 to about 523, inclusive of Figure 160 (SEQ ID NO:282), or (b)

25 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1780 antibody. In yet another embodiment, the invention concerns agonists and amagonists of a native PRO1780

native PRO1780 polypeptide, by contacting the native PRO1780 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide. in a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

30 or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO1780 polypeptide

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35 identity with cerebellin, particularly precerebellin, and designated in the present application as *PRO1486." a PRO1486 polypeptide. In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding A cDNA clone (DNA71180-1655) has been identified that encodes a novel polypeptide having sequence

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule encoding a PRO1486 polypeptide having the sequence of amino acid residues from 1 or about 33 to about 205, inclusive of Figure 162 (SEQ ID NO:287), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1486 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 568 and about 1086, inclusive, of Figure 161 (SEQ ID NO:286). Preferably, hybridization occurs under stringent by bridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 85% sequence identity to (a) a DNA malecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203403 (DNA71180-1655), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203403 (DNA71180-1655).

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In a still further aspect, the invention concerns an isolated mucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 33 to about 205, inclusive of Figure 162 (SEQ ID NO:287), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 melecuides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1486 polypeptide having the sequence of amino acid residues from about 33 to about 205, inclusive of Figure 162 (SEQ ID NO.287), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the armino acid sequence of residues 33 to about 205, inclusive of Figure 162 (SEQ ID NO:287), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1486 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1486 polypeptide encoded by any of the

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isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1486 polypeptide, which in one embodineut, includes an amino acid sequence comprising residues 33 through 205 of Figure 162 (SEQ ID NO:287).

In another aspect, the invention concerns an isolated PRO1486 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to the sequence of amino acid residues 33 to about 205, inclusive of Figure 162 (SEQ ID NO.287).

In a further aspect, the invention concerns an isolated PRO1486 polyperpide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 80% positives, more preferably at least about 80% positives, more preferably at least about 90% positives when compared with the amino acid sequence of residues 33 through 205 of Figure 162 (SEQ ID NO.287).

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In yet another aspect, the invention concerns an isolated PRO1486 polypeptide, comprising the sequence of amino acid residues 33 to about 205, inclusive of Figure 162 (SEQ ID NO:287), or a fragment thereof sufficient to provide a binding site for an anti-PRO1486 antibody. Preferably, the PRO1486 fragment retains a qualitative biological activity of a native PRO1486 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1486 polypeptide having the sequence of amino acid residues from about 33 to about 205, inclusive of Figure 162 (SEQ ID NO:287), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about an 80% sequence

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In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1486
25 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1486 antibody:

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1486 polypoptide, by contacting the native PRO1486 polypoptide with a caudidate molecule and monitoring a biological activity mediated by said polypoptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1486 polypeptide,
Or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

n. PRO1433

A cDNA clone (DNA71184-1634) has been identified that cncodes a novel transmembrane polypeptide designated in the present application as "PRO1433".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO 1433 polypeptide.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity.

preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1433 polypeptide having the sequence of amino acid residues from about 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1433 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 185 and about 1348, inclusive, of Figure 163 (SEQ ID NO:291). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203266 (DNA71184-1634) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203266 (DNA71184-1634).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292), or (b) the complement of the DNA of (a).

In a further espect, the invention concerns an isolated nucleic acid molecule having at least 250 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1433 polypeptide having the sequence of amino acid residues from 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85 % sequence identity, most preferably at least about a 95% sequence identity of (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1433 polypeptide, with or without the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domain has been tentatively identified as extending from about amino acid position 76 to about amino acid position 97 in the PRO1433 amino acid sequence (Figure 164, SEQ ID NO:292).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 388, inclusive of Figure 164 (SEQ ID NO.292), or (b) the complement of the DNA of (s).

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Another embodiment is directed to fragments of a PRO1433 polypeptide coding sequence that may find

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use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 163 (SEQ 1D NO:291).

In another embodiment, the invention provides isolated PRO1433 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

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In a specific aspect, the invention provides isolated native sequence PRO1433 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 388 of Figure 164 (SEQ ID NO:292).

In another aspect, the invention concerns an isolated PRO1433 polypeptide, comprising an amino acid

10 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more
preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
sequence of amino acid residues i to about 388, inclusive of Figure 164 (SEQ ID NO:292).

In a further aspect, the invention concerns an isolated PRO1433 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292).

In yet another aspect, the invention concerns an isolated PRO1433 polypeptide, comprising the sequence of amino acid residues 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292), or a fragment thereof sufficient to provide a binding site for an anti-PRO1433 antibody. Preferably, the PRO1433 fragment retains 20 a qualitative biological activity of a native PRO1433 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1433 polypeptide having the sequence of antino acid residues from about 1 to about 388, inclusive of Figure 164 (SEQ ID NO:292), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about an 85% sequence identity to (a) or (b), (ii) culturing a bost cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1433 0 polypeptide. In a particular embodiment, the agonist or amagonist is an anti-PRO1433 antibody.

polypeptide from the cell culture.

In a further embodiment, the invention concerns a method of identifying aganists or antagonists of a native PRO1433 polypeptide by contacting the native PRO1433 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1433 polypeptide,
35 or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

83. PRO1490

A cDNA clone (DNA71213-1659) has been identified, having homology to nucleic acid encoding a lacyl-an-glycerol-3-phosphate acyltransferase protein that encodes a novel polypeptide, designated in the present
application as "PRO1499".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1490 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1490 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO:297), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1490 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 772 or about 347 and about 1375, inclusive, of Figure 165 (SEQ 1D NO:296). Preferably, hybridization occurs under stringent hybridization and wash conditions.

Is a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 80% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203401 (DNA71213-1659) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the 20 nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203401 (DNA71213-1659).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to the sequence of amino acid residues 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO:297), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 285 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1490 polypeptide having the sequence of amino acid residues from 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO.297), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85 % sequence identity, most preferably at least about a 95 % sequence identity, most preferably at least about a 95 % sequence.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

35 a PRO1490 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and
its soluble, i.e., transmembrane domain deletted or inactivated variants, or is complementary to such encoding

muchic acid molecule. The signal peptide has been tentarively identified as extending from about amino acid

identity to (a) or (b), isolating the test DNA molecule.

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position I to about amino acid position 25 in the sequence of Figure 166 (SEQ ID NO:297). The transmembrane domains have been tentatively identified as extending from about amino acid position 307 to about amino acid position 323 and from about amino acid position 335 to about amino acid position 352 in the PRO1490 amino acid sequence (Figure 166, SEQ ID NO:297).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA 5 encoding a polypoptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 36%, inclusive of Figure 166 (SEQ ID NO:297), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1490 polypeptide coding sequence that may find

10 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50
nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived
from the nucleotide sequence shown in Figure 165 (SEQ ID NO:296).

In another embodiment, the invention provides isolated PRO1490 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

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In a specific aspect, the invention provides isolated native sequence PRO1490 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 26 to about 368 of Figure 166 (SEQ ID NO.297).

In another aspect, the invention concerns an isolated PRO1490 polypeptide, comprising an amino acid
20 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most
preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
sequence of amino acid residues 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO.297).

In a further aspect, the invention concerns an isolated PRO1490 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO:297).

In yet mother aspect, the invention concerns an isolated PRO1490 polypeptide, comprising the sequence of amino acid residues 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO:297), or a fragment theoreof sufficient to provide a binding site for an anti-PRO1490 antibody. Preferably, the PRO1490 fragment 30 retains a qualitative biological activity of a native PRO1490 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) bybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1490 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 368, inclusive of Figure 166 (SEQ ID NO:297), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% contenue identity preferably at least about a 80% contenue identity preferably at least about a 80% contenue identity preferably at least about a 80% contenue.

35 an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii)

recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1490 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1490 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1490 polypeptide by contacting the native PRO1490 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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or an agonist or amagonist as bereinabove defined, in combination with a pharmaceuically acceptable carrier.

PRO148

10 A cDNA clone (DNA71234-1651) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1482".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding 10.1482 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1482 polypeptide having the sequence of amino acid residues from about 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1482

20 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about mucleotides 33 or about 117 and about 461, the husive, of Figure 167 (SEQ ID NO:301), Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203402 (DNA71234-1651) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203402 (DNA71234-1651).

30 In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypepside having at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to the sequence of amino acid residues 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 260 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO 1482 polypeptide having the sequence of antino acid residues from 1 or about 29 to

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about 143, inclusive of Figure 168 (SEQ ID NO: D02), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity in (a) or (b), isolating the test DNA molecule.

In a specific aspear, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1482 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The rignal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 28 in the sequence of Figure 168 (SEQ ID NO:302).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA 10 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1482 polypeptide coding sequence that may find

15 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50
nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived
from the nucleotide sequence abown in Figure 167 (SEQ ID NO:301).

In another embodiment, the invention provides isolated PRO1482 polypeptide encoded by any of the 20 isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1482 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 29 to about 143 of Figure 168 (SEQ ID NO:302).

In mother aspect, the invention concerns an isolated PRO1482 polypeptide, comprising an amino acid
sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more
preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
sequence of amino acid residues 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302).

In a further aspect, the invention concerns an isolated PRO 1482 polypeptide, comprising an amino acid sequence acorting at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302).

In yet another aspect, the invention concerns an isolated PRO1482 polypeptide, comprising the requence of amino acid residues 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:202), or a fragment thereof sufficient to provide a binding site for an anti-PRO1482 antibody. Preferably, the PRO1482 fragment 35 retains a qualitative biological activity of a native PRO1482 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1482 polypeptide having the

sequence of amino acid residues from about 1 or about 29 to about 143, inclusive of Figure 168 (SEQ ID NO:302), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions satiable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1482 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1482 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a mative PRO1482 polypeptide by contacting the native PRO1482 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO 1482 polypeptide, or an agonist or aniagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

PRO1446

15 A cDNA cione (DNA71277-1636) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1446."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO 1446 polyperside.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1446 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 109, inclusive of Figure 170 (SEQ 1D NO:304), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1446 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 197 and about 478, inclusive, of Figure 169 (SEQ ID NO:303). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity to (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203285 (DNA71277-1636), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203285 (DNA71277-1636).

In a still further aspert, the invention concerns an isolated nucleic acid molecule comprising (a) DNA canoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, more preferably at least about 95% sequence.

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identity to the sequence of amino acid residues from about 16 (a about 109, inclusive of Figure 170 (SEQ ID NO:304), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringern conditions with (a) a DNA molecule encoding a PRO 1446 polypeptide having the sequence of amino acid residues from about 16 to about 109, inclusive of Figure 170 (SEQ ID NO:504), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, must preferably at least about a 95% sequence identity, must preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic axid molecule comprising (a) DNA 10 encoding a polypeptide scoring at least about 80% positives, preferably at least about 80% positives, most preferably at least about 90% positives, most preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 16 to about 109, inclusive of Figure 170 (SEQ ID NO:304), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1446 polypeptide coding sequence that may find 15 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1446 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

20 In a specific aspect, the invention provides isolated native sequence PRO1446 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 16 through 109 of Figure 170 (SEQ ID NO:304).

In another aspect, the invention concerns an isolated PRO1446 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to the sequence of amino acid residues 16 to about 109, inclusive of Figure 170 (SEQ ID NO:304).

In a further aspect, the invention concerns an isolated PRO1446 polypeptide, comprising an antito seld sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence 30 of residues 16 through 109 of Figure 170 (SEQ ID NO:304).

In yet another aspect, the invention concerns an isolated PRO1446 polypeptide, comprising the sequence of amino acid residues 16 in about 109, inclusive of Figure 170 (SEQ ID NO:304), or a fragment thereof sufficient to provide a binding site for an anti-PRO1446 antibody. Preferably, the PRO1446 fragment retains a qualitative biological activity of a native PRO1446 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1446 polypeptide having the sequence of animo acid residues from about 16 to about 109, inclusive of Figure 170 (SEQ ID NO:304), or (b)

the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a maive PRO1446 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1446 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1446 polypeptide, by counsering the native PRO1446 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO 1446 polypeptide or an agonist or amagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

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5. PRO1558

A cDNA clone (DNA71282-1668) has been identified, having homology to nucleic acid encoding 15 methyltransferase enzymes that encodes a novel polypeptide, designated in the present application as "PRO1558".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1558 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1538 polypepide having the sequence of amino acid residues from about 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO:306), or (b) the complement of the DNA molecule of (a).

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In another sepect, the invention concerns an isolated nucleic acid molecule encoding a PRO1538 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about mucleoides 84 or about 139 and about 869, inclusive, of Figure 171 (SEQ ID NO:305). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203312 (DNA71282-1668) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203312 (DNA71282-1668).

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In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA caccoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence.

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identity to the sequence of amino acid residues 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO:306), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1538 polypeptide having the sequence of amino acid residues from 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO.306), or (b) the complement of the DNA molecule of (a), and,

about 262, inclusive of Figure 172 (SEQ ID NO.306), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invension provides an isolated nucleic acid molecule comprising DNA emoding

10 a PRO1558 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and
its soluble, i.e., transmembrane domain deleted or inserivated variants, or is complementary to such encoding
nucleic acid molecule. The signal peptide has been remarkedly identified as extending from about amino acid
position 10 about amino acid position 25 in the sequence of Figure 172 (SEQ ID NO-306). The transmembrane
domains have been tentatively identified as extending from about amino acid position 8 to about amino acid
position 30 and from about amino acid position 190 in the PRO1558 amino acid
15 position 30 and from about amino acid position 190 in the PRO1558 amino acid

sequence (Figure 172, SEQ ID NO:306).

La another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA canoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more

preferably at least about 90% positives, most preferably at least about 95% positives when compared with the 20 amino acid sequence of residues 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO:306), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1538 polypeptide coding sequence that may find use as bybridization probes. Such nucleoi and fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 171 (SEQ ID NO:305).

In another embodiment, the invention provides isolated PRO1558 polypoptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1538 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 26 to about 262 of Figure 172 (SEQ ID NO:306

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In another sepect, the invention concerns an isolated PRO 1538 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 83% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 26 to about 262, inclusive of Figure 17(SEQ ID NO;306

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In a further expect, the invention concerns an isolated PRO 1558 polypepide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least

about 99% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 26 to about 262, inclusive of Figure 17(SEQ ID NO:306

In yet another aspect, the invention concerns an isolated PRO1558 polypeptide, comprising the sequence of amino acid restitues 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO:306), or a fragment thereof sufficient to provide a binding site for an anti-PRO1558 antibody. Preferably, the PRO1558 fragment retains a qualitative biological activity of a native PRO1558 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1538 polypeptide having the sequence of amino acid residues from about 1 or about 26 to about 262, inclusive of Figure 172 (SEQ ID NO-306), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a boat 29% sequence identity most preferably at least about a 95% sequence identity to (a) or (b), (iii) culturing a boat cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

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In yet another embodiment, the invention concerns agonists and antegonists of a native PRO1558 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1558 antibody.

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In a further embodiment, the invention concerns a method of identifying agonists or an agonists of a native PRO1558 polypeptide by contacting the native PRO1558 polypeptide with a candidate moticule and mountoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO 1558 polypeptide,
On an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

87. PRO1604

A cDNA clone (DNA71286-1687) has been identified that encodes a novel polypeptide having homology to hepatoma-derived growth factor (HDGF) designated in the present application as "PRO1604".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1604 polypepside.

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In one aspect, the Isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1604 polypeptide having the sequence of amino acid residues from 1 or about 14 to about 671, inclusive of Figure 174 (SEQ ID NO:508), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1604 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 104 and about 2077, inclusive, of Figure 173 (SEQ ID NO:307). Preferably, hybridization occurs under stringent bybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least

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abour 90% sequence identity, most preferably at least abour 95% sequence identity to (a) a DNA molecule encoding the same manue polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203357 (DNA71286-1687), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203357 (DNA71286-1687).

- In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 14 to about 671, inclusive of Figure 174 (SEQ ID NO:308), or the complement of the DNA of (a).
- In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1604 polypeptide having the sequence of amino acid residues from about 14 to about 671, inclusive of Figure 174 (SEQ ID NO:308), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, most preferably at least about a 90% sequence identity, most

preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1604 polypeptide, with or without the N-terminal signal sequence, or it complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position

20 I through about amino acid position 13 in the sequence of Figure 174 (SEQ ID NO:308).
In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 84% positives more

encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 14 to about 671, inclusive of Figure 174 (SEQ ID NO:308), or (b) the 25 complement of the DNA of (a).

- Another embodiment is directed to fragments of a PRO1604 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.
- 30 In another embodiment, the invention provides isolated PRO1604 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO 1604 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 14 to 671 of Figure 174 (SEQ ID NO:308). In another aspect, the invention concerns an isolated PRO 1604 polypeptide, comprising an amino acid

35 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of antino acid residues 14 to about 671, inclusive of Figure 174 (SEQ ID NO:308).

In a further aspect, the invention concerns an isolated PRO1604 polypeptide, comprising an amino acid sequence scoring at least about 80 % positives, preferably at least about 85 % positives, more preferably at least about 90 % positives, mort preferably at least about 90 % positives, mort preferably at least about 90 % positives when compared with the amino acid sequence of residues 14 to 671 of Figure 174 (SEQ ID NO:308).

In yet another aspect, the invention concerns an Isolated PRO1604 polypeptide, comprising the sequence of amino acid residues 14 to about 671, inclusive of Figure 174 (SEO ID NO:308), or a fragment thereof sufficient to provide a binding size for an anti-PRO1604 antibody. Preferably, the PRO1604 fragment retains a qualitative biological activity of a native PRO1604 polypoptide.

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In a still further aspect, the invention provides a polypoptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1664 polypoptide having the 10 sequence of amino acid residues from about 14 to about 671, Inclusive of Figure 174 (SEQ ID NO:308), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity of (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypoptide, and (iii) recovering the 15 polypoptide from the cell culture.

In yet another embodiment, the invention concerns againsts and antagonists of a native PRO1604 polypeptide. In a particular embodiment, the aganist or antagonist is an anti-PRO1604 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1604 polypeptide. by contacting the native PRO1604 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO 1604 polypeptide, or an agonist or amagonist as hereinabove defined, in combination with a pharmacentically acceptable carrier.

88. PRO149

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A cDNA clone (DNA71883-1660) has been identified, having homology to nucleic acid encoding a collapsin protein, that encodes a novel polypeptide, designated in the present application as "PRO1491".

In one embodiment, the invention provides an included models and application as "PRO1491".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1491 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

30 preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most
preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1491 polypeptide having
the sequence of amino acid residues from about 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID

NO:310), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1491
35 polypepide comprising DNA hybridzing to the complement of the nucleic acid between about nucleotides 107
or about 215 and about 2437, inclusive, of Figure 175 (SEQ ID NO:309). Preferably, hybridization occurs
under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 80% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203475 (DNA71883-1660) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203475 (DNA71883-1660).

In still a further aspect, the invention concerns an isolated aucticle acid molecule comprising (a) DNA emodding a polypeptide having at least about 89% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, more preferably at least about 95% sequence.

10 identity to the sequence of anino acid residues 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO:310), or (b) the complement of the DNA of (a).

In a further aspect, the invention concorns an isolated nucleic axid molecule having at least 1,670 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1491 polypeptide having the sequence of amino axid residues from 1 or about 37 to about 777, inclusive of Figure 176 (35Q ID NO:310), or (b) the complement of the DNA molecule of (3), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence

idemity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence

identity to (a) or (b), Isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated modeic acid molecule comprising DNA encoding
20 a PRO1491 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is
complementary to such encoding nucleic acid molecule. The signal peptide has been tentaively identified as
extending from about amino acid position 1 to about amino acid position 36 in the sequence of Figure 176 (SEQ
ID NO:310).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

25 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
amino acid sequence of residues 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO::10), or (b)
the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1491 polypeptide coding sequence that may find 30 use as hybridization probes. Such nucleic neid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 175 (SEQ ID NO:309).

In another embodiment, the invention provides isolated PRO1491 polypeptide encoded by any of the 35 isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the fitteration provides isolated native sequence PRO1491 polypepide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 37 to about 777 of Figure

176 (SEQ ID NO:310).

In another aspect, the invention concerns an isolated PRO1491 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 97 to about 977, inclusive of Figure 176 (SEQ ID NO:510).

In a further aspect, the invention concerns an isolated PRO 1491 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO:310).

In yet another aspect, the invention concerns an isolated PRO1491 polypeptide, comprising the acquence 10 of amino acid residues 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO:310), or a fragment thereof sufficient to provide a binding site for an anti-PRO1491 antibody. Preferably, the PRO1491 fragment retains a qualitative biological activity of a native PRO1491 polypeptide.

In a still further espect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1491 polypeptide having the sequence of amino acid residues from about 1 or about 37 to about 777, inclusive of Figure 176 (SEQ ID NO:310), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity or (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1491 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1491 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1491 polypeptide by contacting the native PRO1491 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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In a still Auther embodiment, the invention concerns a composition comprising a PRO1491 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable earrier.

PR01431

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A cDNA clone (DNA73401-1633) has been identified having a domain with homology to SH3 that encodes a novel polypeptide, which has been designated in the present application as "PRO1431".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1431 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, as preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1431 polypeptide having the sequence of ammo acid residues from about 1 to about 370, inclusive of Figure 178 (SEQ ID NO:315) or

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(b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1431 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between residues 1 to about 1335 and about 1560 to about 3934, inclusive, of Figure 177 (SEQ ID NO:314). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns (a) an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 20273 (DNA73401-1633) or (b) the compilement of the DNA molecule of (a). In a preferred embodiment, the nucleic 10 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 20273 (DNA73401-1633).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% acquence identity, preferably at least about 85% acquence identity, more preferably at least about 90% acquence identity, more preferably at least about 90% acquence identity, more preferably at least about 90% acquence identity to the sequence of amino acid residues from about 1 to about 370, inclusive, of Figure 178 (SEQ ID NO:315), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 15 nucleotides that is produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1431 polypeptide having the sequence of amino acid residues from about 1 to about 20 370, inclusive, of Figure 178 (SEQ ID NO:315), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferrably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

25 encoding a polypoptide scoring at least about 80% positives, preferably at least about 85% positives, more
preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
amino acid sequence of residues 1 to about 370, inclusive, of Figure 178 (SEQ ID NO:315), inclusive, of Figure
178 (SEQ ID NO:315).

In another embodiment, the invention provides isolated PRO1431 polypeptide encoded by any of the 30 isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO [43] polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 370, inclusive, of Figure 178 (SEQ ID NO:315).

In another aspect, the invention concerns an isolated PRO1431 polypeptide, comprising an amino acid

55 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more
preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
sequence of amino acid residues 1 to about 370, inclusive, of Figure 178 (SEQ ID NO:315).

In a further aspect, the invention concerns an isolated PRO1431 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 370 of Figure 178 (SEQ ID NO:315).

In yet another aspect, the invention concerns an isolated PRO1431 or PRO1432 polyperside, comprising the sequence of amino acid residues 1 to about 370, inclusive, or Figure 178 (SEQ ID NO:315), inclusive, of Figure 178 (SEQ ID NO:315), or a fragment thereof sufficient to provide a binding site for an anti-PRO1431 antibody. Preferably, the PRO1431 fragment retains a qualitative biological activity of a native PRO1431 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1431 polypeptide having the sequence of amino acid residues from about 1 to about 370, inclusive, of Figure 178 (SEQ ID NO:315), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity.

15 to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet smather embodiment, the invention concerns agonists and arragonists of a native PRO1431 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1431 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1431 polypeptide, by contacting the native PRO1431 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO1431 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

25 90. PROISG

A cDNA clone (DNA73492-1671) has been identified, having homology to nucleic acid encoding ADAMTS-1 that encodes a novel polypeptide, designated in the present application as "PRO1565".

In one embodiment, the invention provides an isoland nucleic acid molecule comprising DNA encoding PRO 1563 polypeptide.

- 30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 85% sequence identity to (a) a DNA molecule exceeding a PRO1563 polypeptide having the sequence of artino acid residues from about 40 to about 49 to about 837, inclusive of Figure 180 (SEQ ID NO:317), or (b) the complement of the DNA molecule of (a).
- 35 In another aspect, the invention concerns an isolated nucleit acid molecule encoding a PRO1363 polypoptide comprising DNA hybridizing to the complement of the nucleic acid between about mucleonides 419 or about 563 and about 2929, inclusive, of Figures 179A-B (SEQ ID NO.316). Preferably, hybridization occurs

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under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity to (s) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203234 (DNA73492-1671) or (b) the complement of the modelic acid molecule of (a). In a preferred embodiment, the mucleic acid comprises a DNA encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203324 (DNA73492-1671).

In sall a further aspect, the invention conceins an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 85% sequence identity, preferably at least about 85% sequence 10 identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of ambro acid residues 1 or about 49 to about 837, inclusive of Figure 180 (SEQ II) NO:317), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA 15 molecule encoding a PRO1563 polypeptide having the sequence of amino said residues from 1 or about 49 to about 837, inclusive of Figure 180 (SEQ ID NO.317), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferrably at least about an 85% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity to (a) or (b), isolating the test DNA molecule.

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 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1563 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 48 in the sequence of Figure 180 (SEQ ID NO.317).
- In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the armino acid sequence of residues 1 or about 49 to about 837, inclusive of Figure 180 (SEQ ID NO:317), or (b) the complement of the DNA of (a).
- Another embodiment is directed to fragments of a PRO1563 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 90 nucleotides in length and most preferably from about 20 to about 90 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figures 179A-B (SEQ ID NO:316).

 In another embodiment, the invanion provides included PO1464 networked by act of the
- 35 In another embodiment, the invention provides isolated PRO1563 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1563 polypeptide, which in

certain embodiments, includes an amino acid sequence comprising residues 1 or about 49 to about 837 of Figure 180 (SEQ ID NO:317).

In another aspect, the invention concerns an isolated PRO1563 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity in the preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 49 to about 837, inclusive of Figure 180 (SEQ ID NO:317).

In a further aspect, the invention concerns an isolated PRO1563 polypeptide, comprising an amino acid tecquence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 49 to about 497, inclusive of Figure 180 (SEQ ID NO:317).

In yet another aspect, the invention concerns an isolated PRO1563 polypeptide, comprising the sequence of amino acid residues 1 or about 49 to about 837, inclusive of Figure 180 (SEQ 1D NO:317), or a fragment thereof sufficient to provide a binding site for an anti-PRO1563 antibody. Preferably, the PRO1563 fragment retains a qualitative biological activity of a native PRO1563 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA.

15 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1563 polypeptide having the sequence of amino acid residues from about 1 or about 49 to about 837, inclusive of Figure 180 (SEQ ID NO:317), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host 20 cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agenities and amagonists of a native PRO1563 polypeptide. In a particular embodiment, the agenist or antagonist is an anti-PRO1563 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a unive PRO1563 polypeptide by contacting the native PRO1563 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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in a still further embodiment, the invention concerns a composition comprising a PRO 1563 polypeptide, or an agonist or amagonist as bereinabove defined, in combination with a pharmaceutently acceptable currier.

30 91. PRO1565

A cDNA clore (DNA73727-1673) has been identified, having homology to nucleic acid encoding a chandromodulia protein that encodes a novel polypeptide, designated in the present application as "PRO1565". In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1565 polypeptide having

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the sequence of amino acid residues from about 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO.322), or (b) the complement of the DNA molecule of (a).

In another aspect, the inversion concerns an isolated nucleic acid molecule encoding a PRO1565 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 59 or about 179 and about 1009, inclusive, of Figure 181 (SEQ ID NO:321). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein eDNA in ATCC Deposit No. 203459 (DNA73727-1673) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203459 (DNA73727-1673).

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In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence. If identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated molecule having at least 410 mucleoides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA 20 molecule encoding a PRO1365 polypeptide having the sequence of amino acid residues from 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

25 In a specific aspect, the invention provides an isolated nucletic acid molecule comprising DNA encoding a PRO1565 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 40 in the sequence of Figure 182 (SEQ ID NO:322). The transmembrane domain has been tentatively identified as extending from about amino acid position 25 to about amino acid position 47 in the PRO1565 amino acid sequence (Figure 182, SEQ ID NO:322).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the 35 annino acid sequence of residues 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1565 polypeptide coding sequence that may find

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from the nucleotide sequence shown in Figure 181 (SEQ ID NO:321). preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 aucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length

isolated nucleic acid sequences hereinabove identified. In another embodiment, the invention provides isolated PRO1565 polypeptide encoded by any of the

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certain embodiments, includes an amino acid sequence comprising residues 1 or about 41 to about 317 of Figure In a specific aspect, the invention provides isolated native sequence PRO1565 polypeptide, which in

5 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more sequence of amino acid residues 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322), proferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the In another aspect, the invention concerns an isolated PRO1565 polypeptide, comprising an amino acid

5 about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322). sequence scaring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated PRO1565 polypeptide, comprising an amino acid

retains a qualitative biological activity of a native PRO1565 polypeptide. of arnino acid residues 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID NO:322), or a fragment thereof sufficient to provide a binding site for an anti-PRO1565 antibody. Preferably, the PRO1565 fragment In yet another aspect, the invention concerns an isolated PRO 1565 polypeptide, comprising the sequence

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ટ્ટ cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a NO:322), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about sequence of amino acid residues from about 1 or about 41 to about 317, inclusive of Figure 182 (SEQ ID recovering the polypeptide from the cell culture. molecule under stringent conditions with (a) a DNA molecule encoding a PRO1565 polypeptide having the In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

30 polypeptide. In a particular embodiment, the agonist or amagonist is an anti-PRO1565 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1565

native PRO1565 polypeptide by contacting the native PRO1565 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide. In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

35 or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO1565 polypeptide,

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application as "PRO1571". clustridium perfringens enterotoxin receptor (CPE-R) that encodes a novel polypeptide, designated in the present A cDNA clone (DNA73730-1679) has been idemified, having homology to nucleic acid encoding the

a PRO1571 polypeptide In one embodiment, the invention provides an isolated aucleic acid molecule comprising DNA encoding

NO:324), or (b) the complement of the DNA molecule of (a). preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1571 polypeptide having the sequence of amino acid residues from about 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

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or about 153 and about 806, inclusive, of Figure 183 (SEQ ID NO:323). Preferably, hybridization occurs under polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 90 stringent hybridization and wash conditions. In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1571

2 (DNA73T30-1679) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203320 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

8 nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203320 (DNA73730-1679).

25 NO:324), or (b) the complement of the DNA of (a). identity to the sequence of amino acid residues 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence encoding a polypeptide having at least about 80% sequence idently, preferably at least about 85% sequence In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

molecule encoding a PRO1571 polypeptide having the sequence of amino acid residues from 1 or about 22 to nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA in a further aspect, the invention concerns an isolated nucleic acid molecule having at least 910

ಀ about 239, inclusive of Figure 184 (SEQ ID NO:324), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85 % sequence identity to (a) or (b), isolating the test DNA molecule. identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence

ĸ a PRO1571 polypeptide, with or without the N-terminal signal sequence and/or the initiating methlonine, and nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

position 160 to about amino acid position 182 in the PRO1571 amino acid sequence (Figure 184, SEQ ID position 103, from about amino acid position 115 to about amino acid position 141 and from about amino acid domains have been tentatively identified as extending from about amino acid position 82 to about amino acid position 1 to about armino acid position 21 in the sequence of Figure 184 (SEQ ID NO:324). The transmembrane

- preferably it least about 90% positives, most preferably at least about 95% positives when compared with the the complement of the DNA of (a). encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more amino acid sequence of residues 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID NO:324), or (b) In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
- 5 from the nucleotide sequence shown in Figure 183 (SEQ ID NO:323). preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived Another embodiment is directed to tragments of a PRO1571 polypeptide coding sequence that may find
- isolated nucleic acid sequences hereinabove identified. in another embodiment, the invention provides isolated PRO1571 polypeptide encoded by any of the
- certain embodiments, includes an amino acid sequence comprising residues 1 or aboun 22 to about 239 of Figure In a specific aspect, the invention provides isolated untive sequence PRO1571 polypeptide, which in

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- preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more sequence of amino acid residues 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID NO:324). In another aspect, the invention concerns an isolated PRO1571 polypeptide, comprising an amino acid
- 23 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 22 to ahout 239, inclusive of Figure 184 (SEQ ID NO:324). In a further aspect, the invention concerns an isolated PRO1571 polypeptide, comprising an amino acid
- 30 thereof sufficient to provide a binding site for an anti-PRO1571 antibody. Preferably, the PRO1571 fragment of amino acid residues 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID NO:324), or a fragment retains a qualitative biological activity of a native PRO1571 polypeptide. In yet another aspect, the invention concerns an itolated PRO1571 polypeptide, comprising the sequence
- NO:324), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a sequence of amino acid residues from about 1 or about 22 to about 239, inclusive of Figure 184 (SEQ ID molecule under stringent conditions with (a) a DNA molecule encoding a PRO1571 polypeptide having the In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

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90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a bost

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cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1571 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1571

native PRO1571 polypepide by contacting the mative PRO1571 polypepide with a candidate mulecule and monitoring a biological activity mediated by said polypeptide. In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a

or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier in a still further embodiment, the invention concerns a composition comprising a PRO1571 polypeptide

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identity with CPE-R and designated in the present application as "PRO1572." A cDNA clone (DNA73734-1680) has been identified that encodes a novel polypeptide having sequence

la one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

- ᄄ or (b) the complement of the DNA molecule of (a). preferably at least about 95 % sequence identity to (a) a DNA molecule encoding a PRO1572 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most the sequence of amino acid residues from 1 or about 24 to about 261, inclusive of Figure 186 (SEQ ID NO:326), In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity
- 20 hybridization and wash conditions. about 872, inclusive, of Figure 185 (SEQ ID NO:325). Preferably, hybridization occurs under stringent polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 159 and In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1572
- 30 23 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least Deposit No. 203363 (DNA73734-1680). (DNA73734-1680), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203363 in a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having
- 35 NO:326), or the complement of the DNA of (a). encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity to the sequence of amino acid residues from about 24 to about 261, inclusive of Figure 186 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
- nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule baving at least about 50

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preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, amino acid residues from about 24 to about 261, inclusive of Figure 186 (SEQ ID NO:326), or (b) the under stringent conditions with (a) a DNA molecule encoding a PRO1572 polypeptide having the sequence of

domains have been tentatively identified as approximately at about 81-100, 121-141 and 173-194 in the PRO1572 nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding a PRO1572 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and amino acid sequence (Figure 186, SEQ ID NO:326). I through about amino acid position 23 in the sequence of Figure 186 (SEQ ID NO:326). The transmembrane In a specific aspect, the invention provides an isolated ancieic acid molecule comprising DNA encoding

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antino acid sequence of residues 24 to about 261, inclusive of Figure 186 (SEQ ID NO:326), or (b) the encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more complement of the DNA of (a). preferably at least about 90% positives, most preferably at least about 95% positives when compared with the In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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nucleotides in length, and most preferably from about 20 to about 40 nucleotides in tength. preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, Another embodiment is directed to fragments of a PRO1572 polypeptide coding sequence that may find

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isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated PRO1572 polypeptide encoded by any of the

embodiment, includes an amino acid sequence comprising residues 24 through 261 of Figure 186 (SEQ ID In a specific aspect, the invention provides isolated native sequence PRO 1572 polypeptide, which in one

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sequence of amino acid residues 24 to about 261, inclusive of Figure 186 (SEQ ID NO:326). preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more In another aspect, the invention concerns an isolated PRO1572 polypeptide, comprising an amino acid

೪ sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least of residues 24 through 261 of Figure 186 (SEQ ID NO:326). about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence In a further aspect, the invention concerns an isolated PRO1572 polypeptide, comprising an amino acid

35 of amino acid residues 24 to about 261, inclusive of Figure 186 (SEQ ID NO:326), or a fragment thereof sufficient to provide a binding site for an anti-PRO1572 antibody. Preferably, the PRO1572 fragment retains In yet another aspect, the invention concerns an isolated PRO1572 polypeptide, comprising the sequence

a qualitative biological activity of a native PRO1572 polypeptide.

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identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence polypeptide from the cell culture. sequence of amino acid residues from about 24 to about 261, inclusive of Figure 186 (SEQ ID NO:326), or (b) molecule under stringent conditions with (a) a DNA molecule encoding a PRO1572 polypeptide having the In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

polypertide. In a particular embodiment, the agonist or antagonist is an anti-PRO1572 antibody. In yet mother embodiment, the invention concerns agonists and antagonists of a native PRO1572

5 native PRO1572 polypeptide, by contacting the native PRO1572 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide in a further embodiment, the invention concerns a method of identifying agonists or amagonists of a

or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a sill further embodiment, the invention concerns a composition comprising a PRO 1572 polypeptide

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identity with CPE-R and designated in the present application as "PRO1573". A cDNA clone (DNA73735-1681) has been identified that encodes a novel polypeptide having sequence

20 a PRO1573 polypeptide. In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

or (b) the complement of the DNA molecule of (a). the sequence of amino acid residues from 1 or about 18 to about 225, inclusive of Figure 188 (SEQ ID NO:328) preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1573 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity

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hybridization and wash conditions. about 771, inclusive, of Figure 187 (SEQ ID NO:327). Preferably, hybridization occurs under stringent polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 148 and In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1573

š 30 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC (DNA73735-1681), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203356 about 90% sequence identity, most proferably at least about 95% sequence identity to (a) a DNA molecule Deposit No. 203356 (DNA73735-1681). In a further expect, the invention concerns an isolated nucleic acid molecule comprising DNA having

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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NO:328), or the complement of the DNA of (a). identity to the sequence of amino acid residues from about 18 to about 225, inclusive of Figure 188 (SEQ ID encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at Icast about 95% sequence

preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA motecute. nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, amino acid residues from about 18 to about 225, inclusive of Figure 188 (SEQ ID NO:328), or (b) the under stringent conditions with (a) a DNA molecule encoding a PRO1573 polypeptide having the sequence of In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

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I through about amino acid position 17 in the sequence of Figure 188 (SEQ ID NO:328). The transmembrane its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding a PRO1573 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and amino acid sequence (Figure 188, SEQ ID NO:328). domains have been tentatively identified as at approximately 82-101, 118-145 and 164-188 in the PRO1573 nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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20 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more complement of the DNA of (a). amino acid sequence of residues 18 to about 225, inclusive of Figure 188 (SEQ ID NO:328), or (b) the In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length. use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, Another embodiment is directed to fragments of a PRO1573 polypeptide coding sequence that may find

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isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated PRO1573 polypeptide encoded by any of the

30 embodiment, includes an amino acid sequence comprising residues 18 through 225 of Figure 188 (SEQ ID NO:328). in a specific aspect, the invention provides isolated native sequence PRO1573 polypeptide, which in one

sequence of amino acid residues 18 to about 225, Inclusive of Figure 188 (SEQ ID NO:328). preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more In another aspect, the invention concerns an isolated PRO1573 polypeptide, comprising an amino acid

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sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated PRO1573 polypeptide, comprising an arnino acid

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of residues 18 through 225 of Figure 188 (SEQ ID NO:328). about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence

S a qualitative hiological activity of a native PRO1573 polypoptide. sufficient to provide a binding site for an anti-PRO1573 amibody. Preferably, the PRO1573 fragment retains of amino acid residues 18 to about 225, inclusive of Figure 188 (SEQ ID NO:328), or a fragment thereof In yet another aspect, the invention concerns an isolated PRO1573 polypeptide, comprising the sequence

identity, preserably at least about an 85% sequence identity, more preserably at least about a 90% sequence the uest DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture. identity, most preferably at least about a 95 % sequence identity to (a) or (b), (ii) culturing a host cell comprising the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence sequence of amino acid residues from about 18 to about 225, inclusive of Figure 188 (SEQ ID NO:328), or (b) molecule under stringent conditions with (a) a DNA molecule encoding a PRO1573 polypeptide having the In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1573 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1573

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native PRO1573 polypeptide, by contacting the native PRO1573 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide. in a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

20 or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the inversion concerns a composition comprising a PRO1573 polypeptide.

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to Clostridium perfringens enterotoxin receptor (CPE-R), designated in the present application as *PRO1488* A cDNA clone (DNA73736-1657) has been identified that encodes a novel polypeptide having homology

25 a PRO1488 polypeptide. In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

the sequence of amino acid residues from about 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330), or preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1488 polypeptide having preferably at least about 83% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

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(b) the complement of the DNA molecule of (a).

polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 6 and about 665, inclusive, of Figure 189 (SEQ ID NO:329). Preferably, hybridization occurs under stringent la another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1488

at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having 33

hybridization and wash conditions

about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203466 (DNA73736-1657), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203466 (DNA73736-1657).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid testidues from about 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 auxicuities, and preferably at least about 100 mucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1488 polypeptide having the sequence of amino acid residues from about 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity in (a) or (b), isolating the test DNA molecule.

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In a specific aspert, the invention provides an isolated meetic acid molecule comprising DNA encoding a PRO1488 polypeptide, with or without the initiating methionine, and its soluble variates (i.e. transmembrane domains deleted or inactivated), or it complementary to such encoding mucket acid molecule. Transmembrane domains has been tentatively identified as being located as about amino acid positions 8-30, 82-102, [21-140, and 166-186 in the PRO1488 amino acid sequence (Figure 190, SEQ ID NO:330).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the armino acid sequence of residues 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1488 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 40 nucleotides in length,

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In another embodiment, the invention provides isolated PRO1488 polypeptide encoded by any of the isolated mucleic acid sequences hereinabove defined.

embodiment, includes an amino acid sequence comprising residues 1 to 220 of Figure 190 (SEQ ID NO:330).

35 In another aspect, the invention concerns an isolated PRO 1488 polypepilde, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity to the

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sequence of amino acid residues 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330),

In a further aspect, the invention concerns an isolated PRO1488 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 220 of Figure 190 (SEQ ID NO:330).

In yet mother aspect, the invention concerns an isolated PRO1488 polypopoide, comprising the sequence of amino acid residues 1 to about 220, inclusive of Figure 190 (SEQ ID NO:330), or a fragment thereof sufficient to provide a binding site for an anti-PRO1488 antibody. Preferably, the PRO1488 fragment retains a qualitative biological activity of a native PRO1488 polypoptide.

In a still further aspect, the invension provides a polypeptide produced by (i) hybridizing a test DNA 10 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1488 polypeptide having the sequence of amino acid residues from about 1 no about 220, inclusive of Figure 190 (SEQ ID NO:330), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about as 95% sequence identity, more preferably at least about as 95% sequence identity, more preferably at least about as 95% sequence identity, more preferably at least about as 95% sequence identity, more preferably at least about as 95% sequence identity, more preferably at least about as 95% sequence identity, more preferably at least about as 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1488 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1488 antibody.

polypeptide from the cell culture.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a 20 native PRO1488 polypeptide, by contacting the native PRO1488 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a rill further embodiment, the invention concerns a composition comprising a PRO1488 polypeptide or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

25 %. PRO1489

A cDNA clone (DNA73737-1658) has been identified, having homology to nucleic acid encoding the clostridium perfringens enterotoxin receptor (CPE-R) that encodes a novel polypeptide, designated in the present application as "PRO1489".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1489 polypeptide.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1489 polypopulde having the sequence of amino acid residues from about 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332), or 35 (b) the complement of the DNA molecule of (a).

In another expect, the invention concerns an isolated nucleic acid molecule encoding a PRO1489 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 264

and about 782, inclusive, of Figure 191 (SEQ ID NO:331). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein eDNA in ATCC Deposit No. 203412 (DNA73737-1658) or (b) the complement of the nucleic acid notecule of (a). In a preferred embodimon, the nucleic acid comprises a DNA encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203412 (DNA73737-1658).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, to the sequence of amino acid residues 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 25 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1489 polypeptide having the sequence of amino acid residues from 1 to about 173, inclusive of Figure 192 (SEO ID NO:332), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % acquence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% acquence identity on (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1489 polypeptide, with or without the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or it complementary to such encoding nucleic acid molecule. The transmembrane domains have been tentatively identified as extending from about amino acid position 31 to about amino acid position 71 to about amino acid position 90 and from about amino acid position 113 in the PRO1489 amino acid sequence (Figure 192, SEQ ID NO;333).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA cocooling a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more 30 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the armino acid sequence of residues 1 to about 173, inclusive of Figure 192 (SEQ ID KO:332), or (b) the complement of the DNA of (a).

Another embodinear is directed to fragments of a PRO1489 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 191 (SEQ ID NO:331).

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In another embodiment, the invention provides isolated PRO1489 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1489 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 to about 173 of Figure 192 (SEQ ID NO:332).

In another aspect, the invention concerns an isolated PRO1489 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332).

In a further aspect, the invention concerns an isolated PRO1489 polypeptide, comprising an amino acid

10 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 90% positives when compared with the amino acid sequence of residues 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332).

In yet another aspect, the invention concerns an isolated PRO1489 polypeptide, comprising the sequence of amino acid residues 1 to about 173, inclusive of Figure 192 (SEQ ID NO:332), or a fragment thereof 15 sufficient to provide a binding site for an anti-PRO1489 antibody. Preferably, the PRO1489 fragment retains

a qualitative biological activity of a native PRO1489 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1489 polypeptide having the

molecule under stringent conditions with (a) a DNA molecule encoding a PRO1489 polypeptide having the sequence of amino acid residues from about 1 to about 173, inclusive of Figure 192 (SEQ ID NO.332), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at test about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about an 85% sequence identity in (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

25 In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1489 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1489 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a native PRO1489 polypeptide by contacting the native PRO1489 polypeptide with a candidate molecule and reonitoring a biological activity mediated by said polypeptide.

30 In a still further embodiment, the invention concerns a composition comprising a PRO1489 polypeptide, or an agonist or antagonist as betetrabove defined, in combination with a pharmaceutically acceptable carrier.

97. PRO1474

A cDNA clone (DNA73739-1645) has been identified that encodes a novel polypeptide having sequence 35 identity with ovornucoid and designated in the present application as "PRO1474."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1474 polypoptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1474 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 85, inclusive of Figure 194 (SEQ ID NO:334), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1474 polypeptide comprising DNA bybridizing to the complement of the nucleic acid between about residues 102 and about 299, inclusive, of Figure 193 (SEQ ID NO:333). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concirns an isolated nucleic acid molecule comprising DNA having 10 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203270 (DNA73739-1645), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203270 (DNA73739-1645).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA cocording a polyperpride having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of ambo acid residues from about 20 to about 85, inclusive of Figure 194 (SEQ ID NO:334), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1474 polypeptide having the sequence of amino acid residues from about 20 to about 55, inclusive of Figure 194 (SEQ ID NO:334), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about at 80% sequence identity, preferably at least about at 85% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity in (a) or (b), isolating the test DNA molecule.

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypepside scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the armino acid sequence of residues 20 to about 85, inclusive of Figure 194 (SEQ ID NO:334), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1474 polypepoide coding sequence that may find use as hybridization probes. Such mucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1474 polypeptide encoded by any of the

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isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1474 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 20 through 83 of Figure 194 (SEQ ID NO:334).

In another aspect, the invention concerns an itolated PRO1474 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 20 to about 85, inclusive of Figure 194 (SEQ ID NO:334).

In a further aspect, the invention concerns an isolated PRO1474 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 20 through 85 of Figure 194 (SEQ ID NO:334).

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In yet another aspect, the invention concerns an isolated PRO1474 polypeptide, comprising the sequence of amino acid residues 20 to about 85, inclusive of Figure 194 (SEQ ID NO.334), or a fragment thereof sufficient to provide a binding site for an anti-PRO1474 antibody. Preferably, the PRO1474 fragment retains a qualitative biological activity of a native PRO1474 polypeptide.

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In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1474 polypeptide having the sequence of amino acid residues from about 20 to about 85, inclusive of Figure 194 (SEQ ID NO:334), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1474.

25 polypeptide. In a particular embodiment, the agonist or antagonist is an ami-PRO1474 amibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a mative PRO1474 polypeptide, by contacting the native PRO1474 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1474 polypeptide,

30 or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

PRO1508

A cDNA clone (DNA73742-1662) has been identified that encodes a novel secreted polypeptide and designated in the present application as "PRO1508,"

35 In one embodiment, the invention provides an isolated modelic acid molecule comprising DNA encoding a PRO1508 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity

preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1508 polypeptide having the sequence of amino acid residues from 1 or about 31 to about 148, inclusive of Figure 196 (SEQ ID NO:336), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1508 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 160 and about 513, inclusive, of Figure 195 (SEQ ID NO:335). Preferably, thybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated mucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity to (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203316 (DNA73742-1662), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic solid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203316 (DNA73742-1662).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypopoide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 31 to about 148, inclusive of Figure 196 (SEQ ID NO:336), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a tost DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1508 polypeptide having the sequence of amino acid residues from about 31 to about 148, inclusive of Figure 196 (SEQ ID NO:336), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1508 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 30 in the sequence of Figure 196 (SEQ ID NO:336).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to about 148, inclusive of Figure 196 (SEQ ID NO:336), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1508 polypeptide coding sequence that may find

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use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1508 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1508 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 31 to 148 of Figure 196 (SEQ ID NO.336), in another aspect, the invention concerns an isolated PRO1508 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to the sequence of amino acid residues 31 to about 148, inclusive of Figure 196 (SEQ ID NO.336).

In a further aspect, the invention concerns an isolated FRO 1508 polypeptide, comprising un amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, inost preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to 148 of Figure 196 (SBQ ID NO:336).

In yet another aspect, the invention concerns an isolated PRO1508 polypeptide, comprising the sequence of amino acid residues 31 to about 148, inclusive of Figure 196 (SEQ ID NO.336), or a fragment thereof sufficient to provide a binding site for an anti-PRO1508 antibody. Preferably, the PRO1508 fragment retains a qualitative biological activity of a native PRO1508 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA collecule under stringent conditions with (a) a DNA molecule encoding a PRO1508 polypeptide having the sequence of amino acid residues from about 31 to about 148, inclusive of Figure 196 (SEQ ID NO:336), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about an 85% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

99. PRO1555

A cDNA clone (DNA73744-1665) has been identified that encodes a novel transmembrane polypeptide

30 designated in the present application as "PRO1555".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1555 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, to (a) a DNA molecule encoding a PRO1555 polypeptide having the sequence of amino acid residues from 1 or about 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PROJSSS polypeptide comprising DNA bybridizing to the complement of the nucleic acid between about residues 83 and about 827, inclusive, of Figure 197 (SEQ ID NO.337). Preferably, hybridization occurs under stringent bybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203322 (DNA73744-1665), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203322 (DNA73744-1665).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a rest DNA molecule under stringent conditions with (a) a DNA molecule exocoting a PRO 1535 polypeptide having the sequence of amino acid residues from about 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 80% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1555 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble variants (i.e. transmembrane domains deleted or inactivated), or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 31 in the sequence of Figure 198 (SEQ ID NO:338). Two transmembrane domains have been tentatively identified as extending from about amino acid position 1 to about amino acid position 32, and from about amino acid position 195 through about amino acid position 217, in the PRO1555 amino acid sequence (Figure 198, SEQ ID NO:338).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1555 polypepside coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,

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preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1555 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO 1555 polypeptide, which in one

5 embodiment, includes an amino acid sequence comprising residues 32 to 246 of Figure 198 (SEQ ID NO.338).

In another aspect, the invention concerns an isolated PRO 1555 polypeptide, comprising an amino acid
sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more

preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the

sequence of amino acid residues 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338).

10 In a further aspect, the invention concerns an isolated PRO1555 polypeptide, comprising an amino acid sequence acoring at least about 80% positives, perferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 32 to 246 of Figure 198 (SEQ ID NO:338).

In yet another aspect, the invention concerns an isolated PRO1555 polypeptide, comprising the sequence 15 of amino acid residues 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338), or a fragment thereof sufficient to provide a binding site for an anti-PRO1555 antibody. Preferably, the PRO1535 fragment retains a qualitative biological activity of a native PRO1555 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1555 polypeptide having the 20 sequence of amino acid residues from about 32 to about 246, inclusive of Figure 198 (SEQ ID NO:338), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a bost cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the 25 polypeptide from the cell culture.

100. PRO1485

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A cDNA clone (DNA73746-1654) has been identified that encodes a novel polypeptide having sequence identity with lysozyme, and more particularly, lysozyme C precursor, and designated in the present application as "PRO1485."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1485 potypepulde.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1485 polypeptide having the sequence of amino acid residues from 1 or about 19 to about 148, inclusive of Figure 200 (SEQ ID NO:340), or (b) the complement of the DNA molecule of (a).

about 594, inclusive, of Figure 199 (SEQ ID NO:339). Preferably, hybridization occurs under stringent polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 205 and In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1485

Deposit No. 203411 (DNA73746-1654). at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least (DNA73746-1654), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203411 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

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NO:340), or the complement of the DNA of (a). encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence ideralty to the sequence of amino acid residues from about 19 to about 148, inclusive of Figure 200 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most under stringent conditions with (a) a DNA molecule encoding a PRO1485 polypeptide having the sequence of nucleotides, and preferably at least about 100 mucleotides and produced by hybridizing a test DNA molecule amino acid residues from about 19 to about 148, inclusive of Figure 200 (SEQ ID NO:340), or (b) the In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

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25 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more complement of the DNA of (a). amino acid sequence of residues 19 to about 148, inclusive of Figure 200 (SEQ ID NO:340), or (b) the In another aspect, the invention concerns an isolated aucieric acid molecule comprising (a) DNA

preferably from about 20 to about 60 nucleorides in length, more preferably from about 20 to about 50 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length. Another embodiment is directed to fragments of a PRO1485 polypeptide coding sequence that may find

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isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated PRO1485 polypeptide encoded by any of the

embodiment, includes an amino acid sequence comprising residues 19 through 148 of Figure 200 (SEQ ID In a specific aspect, the inversion provides isolated native sequence PRO1485 polypeptide, which in one

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In another aspect, the invention concerns an isolated PRO 1485 polypeptide, comprising an amino acid

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preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 148, inclusive of Figure 200 (SEQ ID NO:340). sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more

about 90 % positives, most preferably at least about 95 % positives when compared with the amino acid sequence sequence scoring at least about 80% positives, preferably ar least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated PRO1485 polypeptide, comprising an amino acid

of residues 19 through 148 of Figure 200 (SEQ ID NO:340).

5 a qualitative biological activity of a native PRO1485 polypeptide. of amino acid residues 19 to about 148, inclusive of Figure 200 (SEQ ID NO:340), or a fragment thereof sufficient to provide a binding site for an anti-PRO1485 ambbody. Preferably, the PRO1485 fragment retains In yet another aspect, the invention concerns an isolated PRO1485 polypeptide, comprising the sequence

5 identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising molecule under stringent conditions with (a) a DNA molecule encoding a PRO1485 polypeptide having the the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence sequence of amino acid residues from about 19 to about 148, inclusive of Figure 200 (SEQ ID NO:340), or (b) In a still further aspect, the invention provides a polypeptide produced by (I) hybridizing a test DNA

polypeptide from the cell culture. the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1485

monitoring a biological activity mediated by said polypeptide. native PRO1485 polypeptide, by contacting the native PRO1485 polypeptide with a candidate molecule and in a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1485 antibody,

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ઇ or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier in a still further embodiment, the invention concerns a composition comprising a PRO1485 polypeptide,

2 PRO1564

30 as *PRO1564*. N-acetylgalactosaminyltransferase protein that encodes a novel polypeptide, designated in the present application A cDNA clour (DNA73760-1672) has been identified, having homology to nucleic acid encoding an

a PRO1564 polypeptide. In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

S, preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1564 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most NO:347), or (b) the complement of the DNA molecule of (a). the sequence of amino acid residues from about 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1564 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 462 or about 546 and about 2378, inclusive, of Figure 201 (SEQ ID NO:346). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity in (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203314 (DNA73760-1672) or (b) the examplement of the nucleic acid molecule of (a). In a preferred embodiment, the madeic acid comprises a DNA encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203314 (DNA73760-1672).

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In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO:347), or (b) the complement of the DNA of (a).

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In a further espect, the invention concerns an isolated nucleic acid molecule having at least 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1564 polypeptide having the sequence of sumino acid residues from 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO:347), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated medeic acid molecule comprising DNA encoding a PRO1564 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or it complementary to such encoding medicic acid molecule. The signal peptide has been tensatively idemified as extending from about amino acid position 28 in the sequence of Figure 202 (SEQ ID NO:347). The transmembrane domain has been tensatively idemified as extending from about amino acid position 10 in the PRO1564 amino acid exquence (Figure 202, SEQ ID NO:347).

30 In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA emoding a polypeptide atoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the armino acid sequence of residues 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO:347), or (b) the complement of the DNA of (a).

Azother embodiment is directed to fragments of a PRO1564 polypeptide coding sequence that may find use as hybridization probes. Such mucleic sold fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50

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nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 201 (SEQ ID NO.346).

In another embodiment, the invention provides isolated PRO1564 polypeptide encoded by any of the isolated nucleic noid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native sequence PRO1564 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 29 to about 639 of Figure 202 (SEQ ID NO.347).

In another aspect, the invention concerns an isolated PRO1564 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO:347).

In a further aspect, the invention concerns an isolated PRO1564 polypeptide, comprising an amino acid sequence scuring at least about 80% positives, preferably at least about 83% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 29 to about 29 to about 639, inclusive of Figure 202 (SEQ ID NO:347).

In yet another aspect, the invention concerns an isolated PRO1564 polypepide, comprising the sequence of amino acid residues 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO;347), or a fragment thereof sufficient to provide a binding site for an ami-PRO1564 antibody. Preferably, the PRO1564 fragment retains a qualitative biological activity of a native PRO1564 polypepide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA 20 molecule under stringent conditions with (a) a DNA molecule encoding a PRO 1564 polypeptide having the sequence of amino acid residues from about 1 or about 29 to about 639, inclusive of Figure 202 (SEQ ID NO 347), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, to (a) or (b), (ii) culturing a host 25 cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1564 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1564 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or anagonists of a 30 native PRO1564 polypeptide by contacting the native PRO1564 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1564 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmacentically acceptable carrier

102. PRO1755

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A cDNA clone (DNA76396-1698) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1755".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

the sequence of amino acid residues from 1 or about 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352) or (b) the complement of the DNA molecule of (a). preferably at least about 95 % sequence identity to (a) a DNA molecule encoding a PRO1755 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most In one aspect, the isolated nucloic acid comprises DNA having at least about 80% sequence identity

hybridization and wash conditions. about 885, inclusive, of Figure 203 (SEQ ID NO:351). Preferably, hybridization occurs under stringent polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 151 and In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1755

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(DNA76396-1698), or (b) the complement of the DNA motecule of (a). In a preferred embodiment, the nucleic Deposit No. 203471 (DNA76396-1698). acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203471 about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule as least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least In a further supect, the invention concerns an isolated nucleic acid molecule comprising DNA having

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8 NO:352), or the complement of the DNA of (a). identity, more preferably at least about 90% requence identity, most preferably at least about 95% sequence encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence idensity to the sequence of amino acid residues from about 32 to about 276, inclusive of Figure 204 (SEQ ID In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DN/

23 under stringent conditions with (a) a DNA molecule encoding a PRO1735 polyproptide having the sequence of preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. preferably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, most complement of the DNA malecule of (a), and, if the DNA malecule has at least about an 80% sequence identity amino acid residues from about 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352), or (b) the nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

30 domain has been tentatively identified as extending from about amino acid position 178 to about amino acid a PRO1755 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and position 198 in the PRO1755 amino acid sequence (Figure 204, SEQ ID NO:352) its soluble variants (i.e. transmembrane domain deleted or inactivated), or is complementary to such encoding l through about amino acid position 31 in the sequence of Figure 204 (SEQ ID NO:352). The transmembrane nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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amino acid sequence of residues 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352), or (b) the preferably at least about 90% positives, most preferably at least about 95% positives when compared with the encoding a polypoptide scoring at least about 80% positives, preferably at least about 85% positives, more

use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleveides in length, and most preferably from about 20 to about 40 nucleosides in length Another embodiment is directed to fragments of a PRO1755 polypeptide coding sequence that may find

isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated PRO1755 polypeptide encoded by any of the

15 10 sequence of amino acid residues 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352). preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the embodiment, includes an amino acid sequence comprising residues 32 to 276 of Figure 204 (SEQ ID NO:352). sequence having at least about 80% sequence identity, proferably at least about 85% sequence identity, more In another aspect, the invention concerns an isolated PRO1755 polypeptide, comprising an amino acid In a specific aspect, the invention provides isolated native sequence PRO1755 polypeptide, which in one

of residues 32 to 276 of Figure 204 (SEQ ID NO:352). about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least la a further aspect, the invention concerns an isolated PRO1755 polypeptide, comprising an amino acid

20 sufficient to provide a binding site for an anti-PRO1755 antibody. Preferably, the PRO1755 fragment retains of amino acid residues 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352), or a fragment thereof a qualitative biological activity of a native PRO1755 polypeptide. In yet another aspect, the invention concerns an isolated PRO1755 polypeptide, comprising the sequence

30 23 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the molecule under stringent conditions with (a) a DNA molecule encoding a PRO1755 polypeptide having the the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence sequence of amino acid residues from about 32 to about 276, inclusive of Figure 204 (SEQ ID NO:352), or (b) identity, most proforably at least about a 95 % sequence identity to (a) or (b), (ii) culturing a host cell comprising identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence In a still further expect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1755 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1755

polypeptide from the cell culture.

35 native PRO1755 polypeptide, by contacting the native PRO1755 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide. In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

In a still further embodiment, the invention concerns a composition comprising a PRO1755 polypeptide

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or an agonist or antagonist as bereinabove defined, in combination with a pharmaceutically acceptable carrier

103. PRO175

A cDNA clone (DNA76398-1699) has been identified that encodes a novel transmembrane polypopide designated in the present application as "PRO1757".

In one embodiment, the invention provides an isolated nucleit acid molecule comprising DNA encoding a PRO1757 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, not preferably at least about 90% sequence identity to (a) a DNA molecule encoding a PRO1757 polypeptide having the sequence of amino acid residues from about 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleit acid molecule encoding a PRO1757 polypeptide comprising DNA bybridizing to the complement of the nucleic acid between about nucleotides 59 or about 116 and about 121, inclusive, of Figure 205 (SEQ ID NO:353). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecute comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecute encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203474 (DNA76398-1699) or (b) the complement of the nucleic acid molecute of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203474 (DNA76398-1699).

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In still a further aspect, the invention concerns an isolated rucleic acid molecule comprising (a) DNA cnooding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to the sequence of amino acid residues 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 125 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1757 polypoptide having the sequence of amino acid residues from 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, prefereably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity (or (a) or (b), isolating the test DNA molecule.

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35 In a specific aspect, the invention provides an isolated meteic acid molecule comprising DNA encoding a PRO1757 polypeptide, with or without the N-terminal signal sequence and/or the initiating methonian, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding

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nucleic acid molecule. The signal popule has been tentatively identified as extending from about amino acid position 1 to about amino acid position 19 in the sequence of Figure 206 (SEQ ID NO:354). The transmembrane domain has been tentatively identified as extending from about amino acid position 91 to about amino acid position 110 in the PRO1757 amino acid sequence (Figure 206, SEQ ID NO:354).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or nbout 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1757 polypeptide coding sequence that may find

10 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length,
preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50
nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived
from the nucleotide sequence shown in Figure 205 (SEQ ID NO:353).

In another embodiment, the invention provides isolated PRO1757 polypeptide encoded by any of the isolated nucleic acid sequences bereinabove identified.

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In a specific supect, the invention provides isolated native sequence PRO1757 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 20 to about 121 of Figure 206 (SEQ ID NO:354).

In another aspect, the invention concerns an isolated PRO1757 polypeptide, comprising an amino acid
20 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more
preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
sequence of amino acid residues 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354).

In a further aspect, the invention concerns an isolated PRO1757 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354).

In yet another aspect, the invention concerns an isolated PRO1757 polypeptide, comprising the sequence of amino acid residues 1 or about 20 to about 121, inclusive of Figure 206 (SEQ ID NO:354), or a fragment thereof sufficient to provide a binding site for an anti-PRO1757 antibody. Preferably, the PRO1757 fragment 30 retains a qualitative biological activity of a native PRO1757 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a rest DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1757 polypeptide having the sequence of amino acid residues from about 1 or about 20 to about 121, Inclusive of Figure 206 (SEQ ID NO:354), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about

35 an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii)

recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1757 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1757 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1757 polypeptide by contacting the native PRO1757 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO 1757 pulypeptide or an agonist or amagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

104: PRO175

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A cDNA close (DNA76399-1700) has been identified that encodes a novel secreted polypeptide designated in the present application as "PRO1758".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1758 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80 % sequence identity, more preferably at least about 90 % sequence identity, more preferably at least about 90 % sequence identity, most preferably at least about 95 % sequence identity to (a) a DNA molecule encoding a PRO1758 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1758

20 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 123 and about 548, inclusive, of Figure 207 (SEQ ID NO:355). Preferably, hybridization occurs under stringent bybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203472 (DNA76399-1700), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203472 (DNA76399-1700).

30 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1758 polypeptide baving the sequence of

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amino acid residues from about 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the text DNA molecule.

In a specific aspect, the invention provides an isolated matlete acid molecule comprising DNA encoding a PRO1738 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tensatively identified as extending from anino acid position 1 through about amino acid position 15 in the sequence of Figure 208 (SEQ ID NO:356).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more 10 preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1758 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, 15 preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 auxileotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1758 polypeptide encoded by any of the isolated nucleic acid sequences bereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1758 polypepide, which in one

20 embodiment, includes an amino acid sequence comprising residues 16 to 157 of Figure 208 (SEQ ID NO.356).

In another aspect, the invention concerns an isolated PRO1758 polypepide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity in the sequence of amino acid residues 16 to about 157, inclusive of Figure 208 (SEQ ID NO.356).

In a further aspect, the invention concerns an isolated PRO1758 polypoptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 16 to 157 of Figure 208 (SEQ ID NO:356).

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In yet another aspect, the invention concerns an isolated PRO1758 polypeptide, comprising the sequence 30 of amino acid residues 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356), or a fragment thereof sufficient to provide a binding site for an anti-PRO1758 aniibody. Preferably, the PRO1758 fragment retains a qualitative biological activity of a native PRO1758 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1758 polypeptide having the 35 sequence of amino acid residues from about 16 to about 157, inclusive of Figure 208 (SEQ ID NO:356), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about a 90% sequence.

identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the lest DNA motecute under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

5. PRO1575

A cDNA clone (DNA76401-1683) has been identified that encodes a novel polypeptide having homology to protein distulfide isomerase and designated in the present application as "PRO1575."

In one embodiment, the invention provides an isolated nucleic acid multicule comprising DNA encoding to 1575 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1575 polypeptide having the sequence of amino acid residues from 1 or about 21 to about 273, inclusive of Figure 210 (SEQ ID NO:338), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1575 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 82 and about 840, inclusive, of Figure 209 (SEQ ID NO:357). Preferably, hybridization occurs under stringent bybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 85% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203360 (DNA76401-1683), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203360 (DNA76401-1683).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 21 to about 273, inclusive of Figure 210 (SEQ ID NO:358), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 mucleotides, and preferably at least about 100 mucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1575 polypepide having the sequence of amino acid residues from about 21 to about 273, inclusive of Figure 210 (SEQ ID NO.358), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific expect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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a PRO1575 polypeptide, its soluble variants, (i.e. transmembrane domain and/or signal peptide deleted or inactivated) or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from artino acid position 1 through about amino acid position 20 in the sequence of Figure 210 (SEQ ID NO:358). The transmembrane domain has been tentatively identified as extending from about amino acid position 143 to about amino acid position 162 in the PRO1575 amino acid sequence (Figure 210, SEQ ID NO:358).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the arnino acid sequence of residues 21 to about 273, inclusive of Figure 210 (SEQ ID NO:358), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1575 polypeptide coding sequence that may find use as hybridization probes. Such nucleic sold fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

15 In another embodiment, the invention provides isolated PRO1575 polypeptide encoded by any of the isolated modele acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO 1575 polypeptide, which in one combodiment, includes an amino acid sequence comprising residues 21 to 273 of Figure 210 (SEQ ID NO:358).

In another aspect, the invention concerns an isolated PRO1575 polypeptide, comprising an amino acid

20 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more
preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
sequence of amino acid residues 21 to about 273, inclusive of Figure 210 (SEQ ID NO:358).

In a further aspect, the invention concerns an isolated PRO1575 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to 273 of Figure 210 (SEQ ID NO:358).

In yet another aspect, the invention concerns an isolated PRO1575 polypeptide, comprising the sequence of amino acid residues 21 to about 273, inclusive of Figure 210 (SEQ ID NO:358), or a fragment thereof sufficient to provide a binding site for an anti-PRO1575 antibody. Preferably, the PRO1575 fragment retains 30 u qualifative biological activity of a native PRO1575 polypeptide.

In a still further aspect, the invention provides a polypertide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1575 polypeptide having the sequence of amino acid residues from about 21 to about 273, inclusive of Figure 210 (SEQ ID NO:358), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about a 90% sequence identity, preferably at least about a 90% sequence.

35 identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions satiable for expression of the polypeptide, and (iii) recovering the

solypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1575 polypeptide. In a particular embodiment, the agonist or naragonist is an anti-PRO1575 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1575 polypeptide, by contacting the native PRO1575 polypeptide with a candidate molecule and memioring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO1575 polypeptide, or an agonds or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

06. PRO178

10 A cDNA clone (DNA76510-2504) has been identified that encodes a novel polypeptide having sequence identity with myelin p0 and designated in the present application as "PRO1787."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding D1787 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule encoding a PRO1787 polypoptide having the sequence of amino acid residues from 1 or about 38 to about 269, inclusive of Figure 212 (SEQ ID NO:364), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1787

20 polypoptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 274 and about 969, inclusive, of Figure 211 (SEQ ID NO:363). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 89% sequence identity, preferably at least about 89% sequence identity, more preferably at least about 99% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203477 (DNA76510-2504), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203477 (DNA76510-2504).

30 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity to the sequence of amino acid residues from about 38 to about 269, inclusive of Figure 212 (SEQ ID NO:364), or the complement of the DNA of (a).

35 In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1787 polypeptide having the sequence of

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amino acid residues from about 38 to about 269, inclusive of Figure 212 (SEQ ID NO.364), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity or (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding 5 a PRO1787 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from aritho acid position 1 through about amino acid position 37 in the sequence of Figure 212 (SEQ ID NO:364). The transmembrane domain has been tentatively identified as extending from about amino acid position 161 through about amino acid position 183 in the PRO1787 amino acid sequence (Figure 212, SEQ ID NO:364).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA cncoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 90% positives, more preferably at least about 90% positives when compared with the armino acid sequence of residues 38 to about 269, inclusive of Figure 212 (SEQ ID NO:364), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1787 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides its lared PRO1787 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

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In a specific aspect, the invention provides isolated native sequence PRO1787 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 38 through 269 of Figure 212 (SEQ ID NO:364).

25 In another aspect, the invention concerns an isolated PRO1787 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 38 to about 269, inclusive of Figure 212 (SEQ ID NO:364).

In a further aspect, the invention concerns an isolated PRO1787 polypeptide, comprising an amino acid
30 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the antino acid sequence
of residues 38 through 269 of Figure 212 (SEQ ID NO:364).

In yet another aspect, the invention concerns an isolated PRO1787 polypeptide, comprising the sequence of amino acid residues 38 to about 269, inclusive of Figure 212 (SEQ ID NO:364), or a fragment thereof sufficient to provide a binding site for an anti-PRO1787 antibody. Preferably, the PRO1787 fragment retains a qualitative biological activity of a native PRO1787 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

molecule under stringent conditions with (a) a DNA molecule encoding a PRO1787 polypeptide having the sequence of amino acid residues from about 38 to about 269, inclusive of Figure 212 (SEQ ID NO.364), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 89% sequence identity, more preferably at least about an 89% sequence identity, more preferably at least about a 99% sequence identity, more preferably at least about a 99% sequence identity, most preferably at least about a 99% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1787 polypepside. In a particular embodiment, the agonist or antagonist is an anti-PRO1787 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1787 polypeptide, by contacting the native PRO1787 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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in a still further embodiment, the invention concerns a composition comprising a PRO1787 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

15 107. PRO1781

A cDNA clone (DNA76522-2500) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1781".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1781 polypeptide.

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In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1781 polypeptide having the sequence of amino acid residues from 1 or about 20 to about 373, inclusive of Figure 214 (SEQ ID NO:366), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1781 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 78 and about 1139, inclusive, of Figure 213 (SEQ ID NO:365). Perferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203469 (DNA76572-2500), or (b) the compilement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203469 (DNA76572-2500).

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence

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identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 20 to about 373, inclusive of Figure 214 (SEQ ID NO:366), or the complement of the DNA of (a).

in a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule concording a PRO1781 polypeptide having the sequence of amino acid residues from about 20 to about 373, inclusive of Figure 214 (SEQ ID NO:36), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about as 80% sequence identity, most preferably at least about as 85% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, to (a) or (b), isolating the text DNA molecule.

10 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1781 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble variants (i.e. transmembrane domain detected or inactivated), or is complementary to such encoding nucleic acid molecule. The signal peptide has been tennuively identified as extending from amino acid position 10 in the sequence of Figure 214 (SEQ ID NO.366). The transmembrane through about amino acid position 19 in the sequence of Figure 214 (SEQ ID NO.366).

position 60 in the PRO1781 amino acid sequence (Figure 214, SEQ ID NO:366).

In mother expect, the invention concerns an isolated modelic acid molecule comprising (a) DNA encoding a polypeptide acorting at least about 80% positives, preferably at least about 85% positives, more

preferably at least about 90% positives, most preferably at least about 95% positives when compared with the 20 amino acid sequence of residues 20 to about 373, inclusive of Figure 214 (SEQ ID NO:366), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1781 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1781 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1781 polypeptide, which in one

30 embodiment, includes an amino acid sequence comprising residues 20 to 373 of Figure 214 (SEQ ID NO:366).
In another aspect, the invention concerns an kolated PRO1781 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 20 to about 373, inclusive of Figure 214 (SEQ ID NO:366).

In a further aspect, the invention concerns an isolated PRO 1781 polypeptide, comprising an amino acid
55 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least
about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence
of residues 20 to 373 of Figure 214 (SEQ ID NO:366).

In yet another aspect, the invention concerns an isolated PRO1781 polypeptide, comprising the sequence of amino acid residues 20 to about 373, inclusive of Figure 214 (SEQ ID NO:366), or a fragment thereof sufficient to provide a binding site for an anti-PRO1781 artibody. Preferably, the PRO1781 fragment retains a qualitative biological activity of a marive PRO1781 polypoptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1781 polypeptide having the sequence of amino acid residues from about 20 to about 373, inclusive of Figure 214 (SEQ 1D NO:366), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about as 90% sequence identity, more preferably at least about as 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

8. PRO155

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A cDNA close (DNA76529-1666) has been identified that emodes a novel transmembrane polypeptide designated in the present application as "PRO1556".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO 1556 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1556 polypeptide having the sequence of amino acid residues from 1 or about 25 to about 269, inclusive of Figure 216 (SEQ ID NO:373), or (b) the complement of the DNA molecule of (a).

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In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1556 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 160 and about 891, inclusive, of Figure 215 (SEQ ID NO:371). Preferably, hybridization occurs under stringent hybridization and weath conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 80% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203315 (DNA76529-1666), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic seld comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203315 (DNA76529-1666).

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
cencoding a polypoptide having at least about 80% sequence identity, proferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 25 to about 269, inclusive of Figure 216 (SEQ ID

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NO:372), or the complement of the DNA of (a).

In a further aspect, the invertion concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1356 polypoptide having the sequence of antino acid residues from about 25 to about 269, inclusive of Figure 216 (SEQ ID NO:372), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about as 80% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), lodating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1556 polypeptide, with or without the N-terminal algual sequence and/or the initiating methioniae, and 10 its soluble variants (i.e. transmembrane domains deletted or hactivated), or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from antito acid position. I through about amino acid position 24 in the acquence of Figure 216 (SEQ ID NO:372). Two transmembrane domains have been tentatively identified as extending from about amino acid position 11 to about amino acid position 25 and from about amino acid position 226 to about amino acid position 243 in the PRO1556 amino acid position 26. SEQ ID NO:372).

In mother aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypopride scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 25 to about 269, inclusive of Figure 216 (SEQ ID NO:372), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1536 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1556 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

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In a specific aspect, the invention provides isolated native sequence PRO1556 polypepide, which in one embodiment, includes an amino acid sequence comprising residues 25 to 269 of Figure 216 (SEQ ID NO.372).

In another aspect, the invention concerns an bolated PRO1556 polymentide committies are existenced.

In another aspect, the invention concerns an isolated PRO1556 polypeptide, comprising an amino acid
30 sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most
preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the
sequence of amino acid residues 25 to about 269, inclusive of Figure 216 (SEQ ID NO:372).

In a further aspect, the invention concerns an isolated PRO1556 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 25 to 269 of Figure 216 (SEQ ID NO:372).

In yet another aspect, the invention concerns an isolated PRO1556 polypeptide, comprising the sequence

of amino acid residues 25 to about 269, inclusive of Figure 216 (SEQ ID NO:372), or a fragment thereot sufficient to provide a hinding site for an anti-PRO1556 amibody. Preferably, the PRO1556 fragment retains a qualitative biological activity of a native PRO1556 polypoptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1556 polypeptide having the sequence of amino acid residues from about 25 to about 269, inclusive of Figure 2.16 (SEQ ID NO:372), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1556 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1556 antibody.

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In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1556 polypeptide, by contacting the native PRO1556 polypeptide with a candidate molecute and monatoring a biological activity mediated by said polypeptide.

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In a still further embodiment, the invention concerns a composition comprising a PRO1556 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

9. PRO175

20 A cDNA clone (DNA/6531-1701) has been identified that encodes a novel polypeptide having multiple transmembrane domains, designated in the present application as "PRO1759."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding PRO1759 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, 25 preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity to (a) a DNA molecule encoding a PRO1759 polypoptide having the sequence of amino acid residues from 1 or about 19 to about 450, inclusive of Figure 218 (SEQ ID NO:374), or (b) the complement of the DNA molecule of (a).

In another expect, the invention concerns an isolated nucleic acid molecule encoding a PRO1759

30 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 179 and about 1474, inclusive, of Figure 217 (SEQ ID NO:373). Preferably, hybridization occurs under stringent bybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic soid molecule comprising DNA having at least about 80% sequence identity, more preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203465 (DNA76531-1701), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic

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acid comprises a DNA encoding the same manure polypoptide encoded by the human protein cDNA in ATCC Deposit No. 203465 (DNA76531-1701).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity, to the sequence of amino acid residues from about 19 to about 450, inclusive of Figure 218 (SEQ ID

NO:374), or the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1759 polypeptide having the sequence of 10 amino acid residues from about 19 to about 450, inclusive of Figure 218 (SEQ ID NO.374), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, professibly at least about an 85% sequence identity, most

preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

15 a PRO1759 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionize, and
its soluble, i.e. transmembrane domains deleted or inactivated variants, or is complementary to such encoding
nucleic acid molecule. The signal peptide has been tensatively identified as extending from amino acid position

1 through about amino acid position 18 in the sequence of Figure 218 (SEQ ID NO:374). The transmembrane
domains have been tentatively identified as being at about amino acids 1-19 (possibly a signal peptide), 41-55,
20 75-94, 127-143, 191-213, 249-270, 278-299, 314-330, 143-359, 379-394, and 410-430 in the PRO1759 amino
acid sequence (Figure 218, SEQ ID NO:374).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the 25 amino acid sequence of residues 19 to about 450, inclusive of Figure 218 (SEQ ID NO:374), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1759 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1759 polypeptide encoded by any of the isolated models acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1759 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 19 through 450 of Figure 218 (SEQ ID NO:374).

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In another supert, the invention concerns an isolated PRO1759 polypeptide, comprising an amino acid sequence having at least about 85% sequence identity, more

preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 19 to about 450, inclusive of Figure 218 (SEQ ID NO:374).

of residues 19 through 450 of Figure 218 (SEQ ID NO:374). about 90 % positives, most preferably at least about 95 % positives when compared with the amino acid sequence sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further expect, the invention concerns an isulated PRO1759 polypeptide, comprising an amino acid

a qualitative biological activity of a native PRO1759 polypeptide. sufficient to provide a binding site for an anti-PRO1759 antibody. Preferably, the PRO1759 fragment retains of amino acid residues 19 to about 450, inclusive of Figure 218 (SEQ ID NO:374), or a fragment thereof In yet another aspect, the invention concerns an isolated PRO1759 polypeptide, comprising the sequence

5 identity, most preferably at least about a 95 % sequence identity to (a) or (b), (ii) culturing a host cell comprising polypeptide from the cell culture. the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence sequence of amino acid residues from about 19 to about 450. inclusive of Figure 218 (SEQ ID NO:374), or (b) invierule under stringent conditions with (a) a DNA molecule encoding a PRO1759 polypepside having the identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

polypoptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1759 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1759

native PRO1759 polypeptide, by contacting the native PRO1759 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide. In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

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or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO1759 polypeptide,

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designated in the present application as "PRO1760." A cDNA clone (DNA76532-1702) has been identified that encodes a novel secreted polypeptide,

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

a PRO1760 polypeptide.

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or (b) the complement of the DNA molecule of (a). preferably at least about 95 % sequence identity to (s) a DNA molecule encoding a PRO1760 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most the sequence of amino acid residues from 1 or about 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376) In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity,

polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 120 and In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1760

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hybridization and wash conditions. about 623, inclusive, of Figure 219 (SEQ ID NO:375). Preferably, hybridization occurs under stringen

encoding the same manure polypeptide encoded by the himan protein cDNA in ATCC Deposit No. 203473 Deposit No. 203473 (DNA76532-1702) acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC (DNA76532-1702), or (b) the complement of the DNA malecule of (a). In a preferred embodiment, the nucleic about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

5 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity to the sequence of amino acid residues from about 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376), or the complement of the DNA of (a). identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

20 15 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, amino acid residues from about 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376), or (b) the under stringent conditions with (a) a DNA molecule encoding a PRO1760 polypeptide having the sequence of In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

23 complement of the DNA of (a). encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376), or (b) the In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length. use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, Another embodiment is directed to fragments of a PRO1760 polypeptide coding sequence that may find

30 isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated PRO1760 polypeptide encoded by any of the

NO:376). embodiment, includes an animo acid sequence comprising residues 21 through 188 of Figure 220 (SEQ ID In a specific aspect, the invention provides isolated native sequence PRO1760 polypeptide, which in one

35 preferably at least abour 90% sequence identity, most preferably at least abour 95% sequence identity to the sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more In another espect, the invention concerns an isolated PRO1760 polypeptide, comprising an amino acid

sequence of amino acid residues 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376).

In a further aspect, the invention concerns an isolated PRO1760 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 21 through 188 of Figure 220 (SEQ ID NO:376).

In yet another aspect, the invention concerns an isolated PRO1760 polypeptide, comprising the sequence of amino acid residues 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376), or a fragment thereof sufficient to provide a binaling site for an anti-PRO1760 antibody. Preferably, the PRO1760 fragment retains a qualitative biological activity of a native PRO1760 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA 10 molecule under stringent conditions with (a) a DNA molecule encoding a PRO1780 polypeptide having the sequence of amino acid residues from about 21 to about 188, inclusive of Figure 220 (SEQ ID NO:376), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, proferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agentists and amagenists of a native PRO1760 polypeptide. In a particular embodiment, the agoust or antagonist is an anti-PRO1760 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or amagonists of a native PRO1760 polypeptide, by contacting the native PRO1760 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

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in a still further embodiment, the invention concerns a composition comprising a PRO1760 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

111. PRO1561

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A cDNA clone (DNA76538-1670) has been identified, having homology to nucleic acid encoding human phospholipase A2 protein that encodes a novel polypeptide, designated in the present application as *PRO1561*.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1561 polyperoide.

30 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1561 polypeptide having the sequence of amino acid residues from about 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378), or (b) the complement of the DNA molecule of (a).

35 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1561 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 29 or about 80 and about 376, inclusive, of Figure 221 (SEQ ID NO:377). Preferably, hybridization occurs under

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stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, enterprising at least about 80% sequence identity in (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203313 5 (DNA76538-1670) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203313 (DNA76538-1670).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA checoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of antito acid residues 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 100 mucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA 15 molecule encoding a PRO1561 polypeptide having the sequence of amino acid residues from 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO.378), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

20 In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1361 polypopide, with or without the N-terminal signal sequence and/or the initiating methloritie, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal poptide has been tentatively identified as extending from about amino acid position 17 in the sequence of Figure 222 (SEQ ID NO:378). The transmembrane domain has been tentatively identified as extending from about amino acid position 1 to about amino acid position.

In another aspect, the invention concerns an Isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the

24 in the PRO1561 amino acid sequence (Figure 222, SEQ ID NO:378).

30 amino acid sequence of residues 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1561 polypoptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and may be derived.

35 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived.

in another embodiment, the invention provides isolated PRO1561 polypeptide encoded by any of the

from the nucleotide sequence shown in Figure 221 (SEQ ID NO:377).

isolated nucleic acid sequences hereinabove identified.

certain embodiments, includes an amino acid sequence comprising residues 1 or about 18 to about 116 of Figure In a specific aspect, the invention provides isolated native sequence PRO1561 polypeptide, which in

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more sequence of amino acid residues 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378). preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the In another aspect, the invention concerns an isolated PRO1561 polypeptide, comprising an amino acid

abour 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378). sequence exoring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated PRO1561 polypeptide, comprising an amino acid

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rctains a qualitative biological activity of a native PRO1561 polypeptide. of amino acid residues 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID NO:378), or a fragment thereof sufficient to provide a binding site for an anti-PRO1561 antibody. Preferably, the PRO1561 fragment In yet another aspect, the invention concerns an isolated PRO 1561 polypeptide, comprising the sequence

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molecule under stringent conditions with (a) a DNA molecule encoding a PRO1561 polypeptide having the In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host recovering the polypeptide from the cell culture. NO:378), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about sequence of amino acid residues from about 1 or about 18 to about 116, inclusive of Figure 222 (SEQ ID

25 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1561 antibody. In yet another embodiment, the invertion concerns agonists and antagonists of a native PRO1561

native PRO1561 polypeptide by contacting the native PRO1561 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide. In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

ઝ or an agonist or antagonist as hereimbove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO1561 polypeptide,

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"PRO1567". to the expression product of the colon specific gene, CSG6, and is designated in the present application as A cDNA clone (DNA76541-1675) has been identified that encodes a novel polypeptide having homology

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In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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a PRO1567 polypeptide.

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or (b) the complement of the DNA molecule of (a). preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1567 polypeptide having preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most the sequence of amino acid residues from 1 or about 23 to about 178, inclusive of Figure 224 (SEQ ID NO:383). In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity

polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 175 and hybridization and wash conditions about 642, inclusive, of Figurc 223 (SEQ ID NO:382). Preferably, hybridization occurs under stringent In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1567

2 5 at teast about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least Deposit No. 203409 (DNA76541-1675). acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC (DNA76541-1675), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203409 about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule In a further aspect, the invention concerns an solated nucleic acid molecule comprising DNA having

NO:383), or the complement of the DNA of (a). encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity to the sequence of amino acid residues from about 23 to about 178, inclusive of Figure 224 (SEQ 1D identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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ટ complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule. preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most amino acid residues from about 23 to about 178, inclusive of Figure 224 (SEQ ID NO:383), or (b) the under stringent conditions with (a) a DNA molecule encoding a PRO1567 polypeptide having the sequence of nucleutides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50

30 nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position a PRO1567 polypeptide, with or without the N-terminal signal sequence, or is complementary to such encoding t through about amino acid position 22 in the sequence of Figure 224 (SEQ ID NO:383). In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

35 amino acid sequence of residues 23 to about 178, inclusive of Figure 224 (SEQ ID NO:383), or (b) the preferably at least about 90% positives, most preferably at least about 95% positives when compared with the encoding a polypeptide securing at least about 80% positives, preferably at least about 85% positives, more complement of the DNA of (a). In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

Another embodiment is directed to fragments of a PRO 1567 polypeptide coding sequence that may find

preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length nucleatides in length, and most preferably from about 20 to about 40 nucleotides in length.

isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated PRO1567 polypeptide encoded by any of the

5 sequence of amino acid residues 23 to about 178, inclusive of Figure 224 (SEQ ID NO:383). embodiment, includes an amino acid requence comprising residues 23 to 178 of Figure 224 (SEQ ID NO:383) preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more In another aspect, the invention concerns an isolated PRO1567 polypeptide, comprising an amino acid In a specific aspect, the invention provides isolated native sequence PRO1567 polypeptide, which in one

of residues 23 to 178 of Figure 224 (SEQ ID NO:383). about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated PRO1567 polypeptide, comprising an amino acid

2 of amino acid residues 23 to about 178, inclusive of Figure 224 (SEQ ID NO:383), or a fragment thereof a qualitative biological activity of a native PRO1567 polypeptide. sufficient to provide a binding site for an anti-PRO1567 antibody. Preferably, the PRO1567 fragment retains In yet mother aspect, the invention concerns an isolated PRO1567 polypeptide, comprising the sequence

25 20 the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the molecule under stringent conditions with (a) a DNA molecule encoding a PRO1567 polypeptide having the polypeptide from the cell culture. the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence sequence of amino acid residues from about 23 to about 178, inclusive of Figure 224 (SEQ ID NO:383), or (b) identity, most preferably at least about a 95 % sequence identity to (a) or (b), (ii) culturing a host cell comprising In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1567 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1567

30 native PRO1567 polypeptide, by contacting the native PRO1567 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

or an agonist or antagonist as hereinabove defined, in combination with a pharmaccutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO1567 polypeptide,

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insulin-like growth factor binding protein that encodes a novel polypeptide, designated in the present application A cDNA clone (DNA77301-1708) has been identified, having homology to nucleic acid encoding an

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In one embodiment, the invention provides an isolated nucleic acid molocule comprising DNA encoding

preferably at least about 95 % sequence identity to (a) a DNA molecule encoding a PRO1693 polypeptide having the sequence of amino acid residues from about 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most NO:385), or (b) the complement of the DNA molecule of (a). In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity

5 or about 607 and about 2046, inclusive, of Figure 225 (SEQ ID NO:384). Preferably, hybridization occurs polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 508 under stringent hybridization and wash conditions. In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1693

encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203407 nucleic acid comprises a DNA encoding the same manne polypopide encoded by the human protein cDNA in (DNA77301-1708) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the ATCC Deposit No. 203407 (DNA77301-1708). about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA moternte at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

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20 encoding a polypepside having at least about 80% sequence identity, preferably at least about 85% sequence NO:385), or (b) the complement of the DNA of (a). idenity to the sequence of amino acid residues 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence In still a further aspect, the invention concerns an isolated nucleic acid motecule comprising (a) DNA

30 23 identity to (a) or (b), isolating the test DNA molecule. if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence molecule encoding a PRO1693 polypeptide having the sequence of amino acid residues from 1 or about 34 to nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA about 513, inclusive of Figure 226 (SEQ ID NO:385), or (b) the complement of the DNA molecule of (a), and, identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 175

35 position I to about amino acid position 33 in the sequence of Figure 226 (SEQ ID NO:385). The transmembrance domain bas been tentatively identified as extending from about amino acid position 420 to about amino acid its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding a PRO1693 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and position 442 in the PRO1693 amino acid sequence (Figure 226, SEQ ID NO:385). nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or ahout 34 to about 513, inclusive of Figure 226 (SEQ ID NO.385), or (b) the complement of the DNA of (a).

- Another embodiment is directed to fragments of a PRO1693 polypeptide coding sequence that may find use at hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 225 (SEQ ID NO:384).
- 10 In another embodiment, the invention provides isolated PRO1693 polypeptide encoded by any of the isolated modele acid sequences hereinabove identified.
- In a specific aspect, the invention provides isolated native sequence PRO1693 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 34 to about 513 of Figure 226 (SEQ JD NO:385).
- In another aspect, the invention concerns an isolated PRO1693 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID NO:385).
- In a further aspect, the invention concerns an isolated PRO1693 polypeptide, comprising an amino acid
 20 sequence souring at least about 80% positives, preferably at least about 85% positives, more preferably at least
 about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence
 of residues 1 or about 34 to about 313, inclusive of Figure 226 (SEQ ID NO:385).
- In yet another aspect, the invention concerns an isolated PRO1693 polypeptide, comprising the sequence of amino acid residues 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID NO:383), or a fragment 25 thereof sufficient to provide a binding site for an anti-PRO1693 arithody. Preferably, the PRO1693 fragment retains a qualitative biological activity of a native PRO1693 polypeptide.
- In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1693 polypeptide having the sequence of amino acid residues from about 1 or about 34 to about 513, inclusive of Figure 226 (SEQ ID 30 NO:385), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.
- In yet another embodiment, the invention concerns agentist and antagenists of a native PRO1693 polypeptide. In a particular embodiment, the agentist or antagenist is an anti-PRO1693 antibody.

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in a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

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native PRO1693 polypeptide by contacting the native PRO1693 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO 1693 polypeptide or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

114. PRO1784

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A cDNA close (DNA77303-2502) has been identified that encodes a novel transmembrane polypeptide designated in the present application as "PRO1784."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1784 polypeptide.

- 10 In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1784 polypeptide having the sequence of amino acid residues from 1 or about 30 to about 146, inclusive of Figure 228 (SEQ ID NO.390), or (b) the complement of the DNA molecule of (a).
- 5 In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1784 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 155 and about 505, inclusive, of Figure 227 (SEQ ID NO:389). Preferably, hybridization occurs under stringent hybridization and wash conditions.
- In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having
 20 at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity most preferably at least about 95% sequence identity to (a) a DNA molecule
 encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203479
 (DNA77303-2502), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic
 acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC
 25 Deposit No. 203479 (DNA77303-2502).
- In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 30 to about 146, inclusive of Figure 228 (SEQ ID NO:390), or the complement of the DNA of (a).
- In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1784 polypoptide having the sequence of amino acid residues from about 30 to about 146, inclusive of Figure 228 (SEQ ID NO:390), or (b) the 35 complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80% sequence identity, more preferably at least about an 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1784 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deletted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 29 in the sequence of Figure 228 (SEQ ID NO:390). The transmembrane domain has been tentatively identified as extending from about amino acid position 52 through about amino acid position 70 in the PRO1784 amino acid sequence (Figure 228, SEQ ID NO:390).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA excoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 30 to about 146, inclusive of Figure 228 (SEQ ID NO:390), or (b) the complement of the DNA of (a)

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Another embodiment is directed to fragments of a PRO1784 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 40 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

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In another embodiment, the invention provides isolated PRO1784 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO1784 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 30 through 146 of Figure 228 (SEQ ID NO:390).

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In another aspect, the invention concerns an isolated PRO1784 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 80% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to the sequence of amino acid residues 30 to about 146, inclusive of Figure 228 (SEQ ID NO:390).

25 In a further aspect, the invention concerns an isolated PRO1784 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 30 through 146 of Figure 228 (SEQ ID NO.390).

In yet another aspect, the invention concerns an isolated PRO1784 polypeptide, comprising the sequence 30 to amino acid residues 30 to about 146, inclusive of Figure 228 (SEQ ID NO:390), or a fragment thereof sufficient to provide a binding site for an anti-PRO1784 amibody. Preferably, the PRO1784 fragment retains a qualitative biological activity of a native PRO1784 polypeptide.

In a still further aspect, the invention provides a polypepside produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1784 polypepside having the 35 sequence of amino acid residues from about 30 to about 146, inclusive of Figure 228 (SEQ ID NO:390), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about a 90% sequence

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identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodimens, the invention concerns agonists and antagonists of a native PRO1784 polypoptide. In a particular embodimens, the agonist or antagonist is an anti-PRO1784 antibody.

5 In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1784 polypeptide, by consucting the native PRO1784 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO 1784 polypeptide or an agonist or antagonist as bereinabove defined, in combination with a pharmaceutically acceptable carrier

115. PRO1605

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A cDNA clore (DNA77648-1688) has heen identified, having homology to nucleit acid encoding a glycosyltransferase protein that encodes a novel polypeptide, designated in the present application as "PRO1605".

15 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1605 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1605 polypeptide having the sequence of amino acid residues from about 1 or about 27 to about 140, inclusive of Figure 230 (3EQ ID).

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NO:395), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1605 polypepide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 425 polypepide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 425 or about 503 and about 844, inclusive, of Figure 229 (SEQ ID NO:394). Preferably, hybridization occurs under

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stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule exceding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit 203408

30 (DNA77648-1688) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203408 (DNA77648-1688).

In still a further aspect, the invention concerns an isolated modele acid molecule comprising (a) DNA encoding a polypoptide having at least about 80% sequence identity, preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO.395), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 380 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1605 polypeptide having the sequence of amino acid residues from 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferrably at least about an 85 % sequence identity, more preferrably at least about a 90 % sequence identity or (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1605 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 26 in the sequence of Figure 230 (SEO ID NO-205).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, prettrably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1605 polypeptide coding requerce that may find use as hybridization probes. Such mucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 229 (SEQ ID NO:394).

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In another embodiment, the invention provides isolated PRO1605 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

In a specific aspect, the invention provides isolated native acquence PRO1605 polypeptide, which in certain embodiments, includes an armino acid sequence comprising residues 1 or about 27 to about 140 of Figure 230 (SEQ ID NO:395).

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In another aspect, the invention concerns an isolated PRO1605 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to the sequence of amino acid residues 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395).

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In a further aspect, the invention concerns an isolated PRO1605 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 80% positives, more preferably at least about 90% positives when compared with the amino acid sequence of residues 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395).

35 In yet another aspect, the invention concerns an isolated PRO1605 polypeptide, comprising the sequence of amino acid residues 1 or about 27 to about 140, inclusive of Figure 230 (SEQ ID NO:395), or a fragment thereof sufficient to provide a binding site for an anti-PRO1605 antibody. Preferably, the PRO1605 fragment

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retains a qualitative biological activity of a native PRO1605 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1605 polypeptide having the sequence of amino acid residues from about 1 or about 27 to about 140, inclusive of Figure 220 (SEQ ID NO:395), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about an 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the pulypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1605

10 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1605 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or anagonists of a maive PRO1605 polypeptide by contacting the native PRO1605 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1605 polypeptide,

15 or an agonist or antagonist as thereinabove defined, in combination with a pharmaceutically acceptable carrier,

116. PRO1788

A cDNA clone (DNA77652-2505) has been identified that encodes a novel polypeptide having homology to leutine-tich repeat proteins and designated in the present application as "PRO1788."

20 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1788 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA nuclecule encoding a PRO1788 polypeptide having the sequence of amino acid residues from 1 or about 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397),

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or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule emoding a PRO1788 polypeptide comprising DNA hybridizing to the compilement of the nucleic acid between about residues 112 and about 1122, inclusive, of Figure 231 (SEQ ID NO:396). Preferably, hybridization occurs under stringent 30 hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203480

35 (DNA77652-2505), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203480 (DNA77652-2505).

In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397), or the complement of the DNA of (a).

In a further supect, the invention concerns an isolated nucleic acid molecule having at least about 30 nucleoxides, and preferably at least about 100 nucleoxides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1788 polypeptide having the sequence of amino acid residues from about 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about a 80% sequence identity, preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1788 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e. transmembrane domain deleted or iractivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from amino acid position 1 through about amino acid position 16 in the sequence of Figure 222 (SEQ ID NO;397). Transmembrane domains have been tentatively identified as extending from about amino acid position 215 through about amino acid position 212 and about amino acid position 287 through about amino acid position 304 in the PRO1788 amino acid sequence (Figure 232, SEQ ID NO;397).

In another aspect, the invention concerns an isolated mudeix axid molecule comprising (a) DNA encoding a polypeptide acoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the armino acid sequence of residues 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397), or (b) the complement of the DNA of (a).

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Another embodiment is directed to fragments of a PRO1788 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length,

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In another embodiment, the invention provides isolated PRO1788 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

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In a specific aspect, the invention provides isolated native sequence PRO1788 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 17 to 353 of Figure 232 (SEQ ID NO:397).

In another aspect, the invention concerns an isolated PRO1788 polypeptide, comprising an amino acid

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 17 to about 353, inclusive of Figure 232 (SEQ ID NO.397).

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In a further aspect, the invention concerns an isolated PRO1788 polypeptide, comprising an amino acid

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sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 17 to 353 of Figure 232 (SEQ ID NO:397).

In yet another aspect, the invention concerns an isolated PRO1788 polypeptide, comprising the sequence of amino acid residues 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397), or a fragment thereof sufficient to provide a binding site for an ani-PRO1788 antibody. Preferably, the PRO1788 fragment retains

a qualitative biological activity of a native PRO1788 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1788 polypeptide having the sequence of amino acid residues from about 17 to about 353, inclusive of Figure 232 (SEQ ID NO:397), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 85% sequence identity, preferably at least about an 85% sequence identity, preferably at least about an 85% sequence.

10 the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity, most preferably at least about a 90% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1788 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1788 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1788 polypeptide, by contacting the native PRO1788 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

20 In a still further embodiment, the invention concerns a composition comprising a PRO1788 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

117. PRO1801

A cDNA clone (DNA83XW-2506) has been identified, having homology to nucleic acid encoding 1L-19
25 polypeptide, that encodes a novel polypeptide, designated in the present application as "PRO1801".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1801 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1801 polypeptide having the sequence of amino acid residues from about 4 or about 43 to about 261, inclusive of Figure 234 (SEQ ID

NO:402), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an balancd mucleic acid molecule encoding a PRO1801 polypeptide compristing DNA hybridizing to the complement of the nucleic acid between about medicoides 109 or about 235 and about 891, inclusive, of Figure 233 (SEQ ID NO:401). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule about 90% sequence identity to (b) a DNA molecule encoding the same mature polypeptide encoded by the human protein eDNA in ATCC Deposit No. 203391 (DNA83500-2506) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203391 (DNA83500-2506).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA cncoding a polypeptide having at least about 80% sequence identity, preferably at least about 95% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino axid residues 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 30 nucleotides, usually at least about 100 nucleotides and generally at least about 100 nucleotides and generally at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1801 polypeptide having the sequence of amino acid residues from 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, most preferably at least about a 95 % sequence identity, most preferably at least about a 95 %.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding 20 a PRO 1801 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 42 in the sequence of Figure 234 (SEQ ID NO:402).

sequence identity to (a) or (b), isolating the test DNA molecule.

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA
25 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more
preferably at least about 90% positives, most preferably at least about 95% positives when compared with the
amino acid sequence of residues 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402), or (b)
the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1801 polypeptide coding sequence that may find 30 use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 233 (SEQ ID NO:401).

In another embodiment, the invention provides isolated PRO1801 polypeptide encoded by any of the isolated nucleic acid sequences bereinabove identified.

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la a specific espect, the invention provides isolated native sequence PRO1801 polypeptide, which in tertain embodiments, includes an amino acid sequence comprising residues 1 or about 43 to about 261 of Figure

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234 (SEQ ID NO:402)

In another aspect, the invention concerns an isolated PRO1801 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402).

in a further aspect, the invention concerns an isolated PRO1801 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402).

In yet another aspect, the invention concerns an isolated PRO1801 polypepide, comprising the sequence
10 of amino acid residues 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402), or a fragment
thereof sufficient to provide a binding site for an anti-PRO1801 antibody. Preferably, the PRO1801 fragment
retains a qualitative biological activity of a native PRO1801 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1801 polypeptide having the sequence of amino acid residues from about 1 or about 43 to about 261, inclusive of Figure 234 (SEQ ID NO:402), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about as 80% sequence identity, preferably at least about as 85% sequence identity, most preferably at least about as 90% sequence identity, most preferably at least about as 95% sequence identity to (a) or (b), (ii) culturing a bost cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the lavention concerns agonists and antagonists of a native PRO1801 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1801 antibody:

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1801 polypeptide by contacting the native PRO1801 polypeptide with a candidate molecule and 25 monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1801 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

Another embodiment of the present invention is directed to a method of inhibiting the production of an

inflammatory cytokine by a cell capable of producing that inflammatory cytokine, wherein the method comprises

the step of contacting the cell with a PRO 1801 polypeptide, wherein the production of the inflammatory cytokine
is inhibited. The cell may be, for example, a T-cell, an NK cell or a macrophage and the inflammatory cytokine
whose production is inhibited may be, for example, IL-1. IL-6, IFN-y or TNF-a.

A further embodiment of the present invention is directed to a method for the treatment of an individual in need of immunosuppression, wherein the method comprises the step of administering to the individual an immunosuppressive amount of a PRO1801 polypeptide. The individual in need of immunosuppression may suffer from an autoimmune disease, such as rheumatoid arthritis, myasthenia gravis, insulin-dependent diabetes melitus, systemic lupus erythematosus, thorothesis or collisis, or from septic shock, endotoxic shock or any other

to receive a tissue transplant, where the method serves to inhibit rejection of the tissue transplant. type of disorder where immunosuppression is desired. The individual may also be one who has received or is

Other embodiments will become evident upon a reading of the present specification.

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uncoupling proteins, that encodes a novel polypeptide, designated in the present application as "UCPA," A cDNA clone (DNA77568-1626) has been identified, having certain homologies to some known human

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

5 preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most the complement of the DNA molecule of (a). preferably at least about 95% acquence identity to (a) a DNA molecule encoding a UCP4 polypeptide having the sequence of amino acid residues from about 1 to about 323, inclusive of Figure 236 (SEQ ID NO:406), or (b) In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity

comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 40 and about 1011 inchusive, of Figure 235 (SEQ ID NO:405). Preferably, hybridization occurs under stringent hybridization and In another aspect, the invention concerns an isolated nucleic acid molecule encoding a UCP4 polypeptide

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z 20 a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic soid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203134. encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203134, or at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

30 encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 323, inclusive of Figure 236 (SEQ ID NO:406), or (b) the In another aspect, the invention concerns an isolated nucleic acid motecute comprising (a) DNA

complement of the DNA of (a).

sequence of ammo acid residues from about 1 to about 323, inclusive of Figure 236 (SEQ ID NO:406), or the

35 Further embodiments of the invention are directed to fragments of the UCP4 coding sequence, which

complement of the DNA of (a).

to about 80 consecutive bases included in the sequence of Figure 235 (SEQ ID NO:405). Optionally, such are sufficiently long to be used as hybridization probes. Preferably, such fragments contain at least about 20 fragments include the N-terminus or the C-terminus of the sequence of Figure 236 (SEQ ID NO:406)

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isolated nucleic acid sequences hereinabove defined. In another embodiment, the invention provides isolated UCP4 polypeptide encoded by any of the

embodiment, includes an amino acid sequence comprising residues 1 to 323 of Figure 236 (SEQ ID NO:406). In another aspect, the invention concerns an isolated UCP4 polypeptide, comprising an amino acid In a specific aspect, the invention provides isolated native sequence UCP4 polypeptide, which in one

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 323, inclusive of Figure 236 (SEQ ID NO:406).

about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 323 of Figure 236 (SEQ ID NO:406). sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least In a further aspect, the invention concerns an isolated UCP4 polypeptide, comprising an amino acid

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retains at least one biological activity of a native UCP4 polypeptide. of amino acid residues 1 to about 323, inclusive of Figure 236 (SEQ ID NO:406), or a fragment thereof sufficient to, for instance, provide a binding site for an anti-UCP4 antibody. Preferably, the UCP4 fragment In yet another aspect, the invention concerns an isolated UCP4 polypeptide, comprising the sequence

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20 identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the of amino acid residues from about 1 to about 323, inclusive of Figure 236 (SEQ ID NO:406), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a bost cell comprising molecule under stringent conditions with (a) a DNA molecule encoding a UCP4 polypeptide having the sequence In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

25 polypeptide. In a particular embodiment, the agonist or amagonist is an anti-UCP4 antibody. In yet another embodiment, the invention concerns agonists and antagonists of the native UCPs

the desired activity. The invention also provides therapeutic methods and diagnostic methods using UCP4. native UCP4 polypeptide, by contacting the native UCP4 polypeptide with a candidate molecule and monitoring In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

30 or an agonist or amagonist as hereinabove defined, in combination with a carrier In a still further embodiment, the invention concerns a composition comprising a UCP4 polypeptide

119. PRO193

polypeptide, designated in the present application as "PRO193," A cDNA clone (DNA23322-1393) has been identified that encodes a novel multi-transmembrane

35 a PRO193 polypeptide. In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

In one aspect, the koleted nucleic acid comprises DNA having at least about 80% sequence identity,

preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO193 polypeptide having the sequence of amino acid residues from about 1 to about 158, inclusive of Figure 238 (SEQ ID NO:410), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO193 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 138 and about 611, inclusive, of Figure 237 (SEQ ID NO:409). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, most preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule emoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No.203400 (DNA23322-1393), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA emodding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203400 (DNA23322-1393).

15 In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the requence of amino acid residues from about 1 to about 158, inclusive of Figure 238 (SEQ ID NO:410), or the complement of the DNA of (a).

20 In a further aspect, the invention concerns an isolated nucleic acid molecule produced by hybridising a test DNA molecule under suringers conditions with (a) a DNA molecule encoding a PRO193 polypeptide having the sequence of amino acid residues from about 1 to about 158, inclusive of Figure 238 (SEQ ID NO:410), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85 % sequence identity, more preferably at least about a 95 % sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO193 polypeptide in its soluble form, i.e. transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The transmembrane domain has been tentatively identified as extending from about amino acid positions 22-42, 60-80, 97-117 and 128-148 in the PRO193 amino acid sequence (Figure 238, SEQ ID NO:410).

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In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide acoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, more preferably at least about 90% positives, more preferably at least about 90% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to about 158, inclusive of Figure 238 (SEQ ID NO:410), or (b) the complement of the DNA of (a).

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In another embodiment, the invention provides isolated PRO193 polypeptide encoded by any of the

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isolated nucleic acid sequences hereinabove defined.

In a specific aspect, the invention provides isolated native sequence PRO193 polypeptide, which in one emboditnem, includes an amino acid sequence comprising residues 1 through 158 of Figure 238 (SEQ ID NO.410).

In another aspect, the invention concerns an isolated PRO193 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 to about 158, inclusive of Figure 238 (SEQ 1D NO:410).

In a further aspect, the invention concerns an isolated PRO193 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives when compared with the amino acid sequence of residues 1 durough 158 of Figure 238 (SEQ ID NO:410).

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO193 polypeptide having the sequence of amino acid residues from about 1 to about 158, inclusive of Figure 238 (SEQ ID NO:410), or (b) 15 the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, more preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the

20 In yet another embodiment, the invention concerns agonists and antagonists of the a native PRO193 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO193 antibody.

polypeptide from the cell culture.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO193 polypeptide, by contacting the native PRO193 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

25 In a still further embodiment, the invention concerns a composition comprising a PRO193 polypeptide, or an agonist or antagonist as herethabove defined, in combination with a pharmaceutically acceptable carrier.

120. PRO113

A cDNA clone (DNA59814-1486) has been identified, having homology to nucleic acid encoding the 30 human 2-19 protein that encodes a novel polypeptide, designated in the present application as "PRO1130".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA exceeding a PRO1130 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 90% sequence identity, preferably at least about 90% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1130 polypeptide having the sequence of antino acid residues from about 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID NO:415), or (b) the complement of the DNA molecule of (a).

or about 357 and about 983, inclusive, of Figure 239 (SEQ ID NO:414). Preferably, hybridization occurs under polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 312 stringent hybridization and wash conditions. in another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1130

ATCC Deposit No. 203359 (DNA59814-1486). at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in (DNA59814-1486) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule eacoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203359 In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having

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NO:415), or (b) the complement of the DNA of (a). identity to the sequence of amino acid residues 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DN/

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if the DNA molecule has at least about an 80 % sequence identity, prefereably at least about an 85% sequence identity to (a) or (b), isolating the test DNA molecule. identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence about 224, inclusive of Figure 240 (SEQ ID NO:415), or (b) the complement of the DNA molecule of (a), and molecule encoding a PRO1130 polypeptide having the sequence of amino acid residues from 1 or about 16 to nucleotides and produced by hybridizing a rest DNA molecule under stringers conditions with (a) a DNA In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10

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extending from about amino acid position 1 to about amino acid position 15 in the sequence of Figure 240 (SEQ complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as a PRO1130 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, or is ID NO:415) In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding

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preferably at least about 90% positives, most preferably at least about 95% positives when compared with the the complement of the DNA of (a). encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more amino acid sequence of residues 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID NO:415), or (b) In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA

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preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 from the nucleotide sequence shown in Figure 239 (SEQ ID NO:414). Another embodiment is directed to fragments of a PRO1130 polypeptide coding sequence that may find

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use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleorides in length, nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived

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isolated nucleic acid sequences hereinabove identified. in another embodiment, the invention provides isolated PRO1130 polypeptide encoded by may of the

certain embodiments, includes an amino acid sequence comprising residues 1 or about 16 to about 224 of Figure In a specific aspect, the invention provides isolated native sequence PRO1130 polypeptide, which in

sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more sequence of amino acid residues I or about 16 to about 224, inclusive of Figure 240 (SEQ ID NO:415). preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the In another aspect, the invention concerns an isolated PRO1130 polypeptide, comprising an amino acid

5 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least of residues 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID NO:415). abour 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence In a further aspect, the invention concerns an isolated PRO1130 polypeptide, comprising an amino acid

15 thereof sufficient to provide a binding site for an anti-PRO1130 antibody. Preferably, the PRO1130 fragment retains a qualitative biological activity of a native PRO1130 polypeptide. of amino acid residues 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID NO:415), or a fragment In yet another aspect, the invention concerns an isolated PRO1130 polypeptide, comprising the sequence

molecule under stringent conditions with (a) a DNA molecule encoding a PRO1130 polypeptide having the In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

20 NO:415), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a recovering the polypeptide from the cell culture. sequence of amino acid residues from about 1 or about 16 to about 224, inclusive of Figure 240 (SEQ ID

23 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1130 antibody. In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1130

monitoring a biological activity mediated by said polypeptide. native PRO1130 polypeptide by contacting the native PRO1130 polypeptide with a candidate molecule and In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a

30 or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier In a still further embodiment, the invention concerns a composition comprising a PRO1130 polypeptide

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ž carbonic unhydrase that encodes a novel polypeptide, designated in the present application as "PRO1335" In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding A cDNA clone (DNA62812-1594) has been identified, having homology to nucleic acid encoding

a PRO1335 polypepide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1335 polypeptide having the sequence of amino acid residues from about 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO-423), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1335 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 271 or about 316 and about 1281, inclusive, of Figure 241 (SEQ ID NO:422). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203248 (DNA62812-1594) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203248 (DNA62812-1594).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423), or (b) the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 180 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1335 polypeptide having the sequence of amino acid residues from 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, profereably at least about an 85% sequence identity, most preferably at least about a 95% sequence identity (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1335 polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and 30 its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 15 in the sequence of Figure 242 (SEQ ID NO:423). The transmembrane domain has been tentatively identified as extending from about amino acid position 291 to about amino acid position 310 in the PRO1335 amino acid sequence (Figure 242, SEQ ID NO:423).

35 In another aspect, the invention concerns an isolated aucieic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the

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amino acid sequence of residues 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423), or (b) the complement of the DNA of (s).

Another embodimen is directed to fragments of a PRO1335 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived

from the nucleotide sequence shown in Figure 241 (SEQ ID NO.422).

In another embodiment, the invention provides isolated PRO1335 polypeptide encoded by any of the

isolated nucleic acid sequences hereinabove identified

In a specific aspect, the invention provides isolated native sequence PRO1335 polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 16 to about 337 of Figure 242 (SEO ID NO:423).

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In another aspect, the invernion concerns an isolated PRO1335 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423).

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In a further aspect, the invention concerns an isolated PRO1335 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 95% positives, more preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423).

20 In yet another aspect, the invention concerns an isolated PRO1335 polypeptide, comprising the sequence of amino acid residues 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423), or a fragment thereof sufficient to provide a binding site for an anti-PRO1335 antibody. Preferably, the PRO1335 fragment retains a qualitative biological activity of a native PRO1335 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1335 polypeptide having the exquence of amino acid residues from about 1 or about 16 to about 337, inclusive of Figure 242 (SEQ ID NO:423), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) culturing a host occll comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1335 polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1335 antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a 35 native PRO1335 polypeptide by contacting the native PRO1335 polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodimera, the invention concerns a composition comprising a PRO1335 polypeptide

or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier

122. PROIX

A cDNA clone (DNA66660-1585) has been identified that encodes a novel polypeptide designated in the present application as "PRO1329."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1329 polymeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1329 polypeptide having the sequence of amino acid residues from 1 or about 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429), or (b) the complement of the DNA molecule of (a).

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In another expect, the invention concerns an isolated nucleic acid molecule encoding a PRO1329 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 138 and about 716, inclusive, of Figure 243 (SEQ ID NO:428). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203279 (DNA66660-1585), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203279 (DNA66660-1585).

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues from about 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule nucleotides and produced by hybridizing a test DNA molecule monding a PRO1329 polypeptide having the sequence of animo acid residues from about 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429), or (h) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about at 80% sequence identity, more preferably at least about at 80% sequence identity, most preferably at least about at 95% sequence identity, most preferably at least about at 95% sequence identity, most preferably at least about at 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated medeic acid molecule comprising DNA encoding a PRO1329 polypepside, with or without the N-terminal signal sequence and/or the imitating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been ternatively identified as

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extending from amino acid position 1 through about amino acid position 16 in the sequence of Figure 244 (SEQ ID NO:429).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 90% positives, most preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 17 to about 209, inclusive of Figure 244 (SEQ ID NO-429), or (b) the

Another embodiment is directed to fragments of a PRO 1329 polypoptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embediment, the invention provides isolated PRO1329 polypsytide encoded by any of the isolated nucleic acid sequences hereimabove defined.

In a specific aspect, the invention provides isolated native sequence PRO 1329 polypeptide, which in our embodiment, includes an amino acid sequence comprising residues 17 to 209 of Figure 244 (SEQ ID NO:429).

In another aspect, the invention concerns an isolated PRO1329 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429).

In a further aspect, the invention concerns an isolated PRO1329 polypeptide, comprising an amino acid
20 sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 17 to 209 of Figure 244 (SEQ ID NO:429).

In yet another aspect, the invention concerns an isolated PRO1329 polypeptide, comprising the sequence of amino acid residues 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429), or a fragment thereof So sufficient to provide a binding site for an anti-PRO1329 antibody. Preferably, the PRO1329 fragment retains a qualitative biological activity of a native PRO1329 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1329 polypeptide having the sequence of amino acid residues from about 17 to about 209, inclusive of Figure 244 (SEQ ID NO:429), or (b) 30 the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, more preferably at least about an 80% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity, more preferably at least about a 90% sequence identity to (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the

123. PRO1550

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polypeptide from the cell culture.

A cDNA clone (DNA76393-1664) has been identified that encodes a novel secreted polypeptide and

designated in the present application as "PRO1550."

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding R01550 polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1550 polypoptide having the sequence of smino acid residues from 1 or about 31 to about 243, inclusive of Figure 246 (SEQ ID NO.431), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1550 polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about residues 228 and about 866, inclusive, of Figure 245 (SEQ ID NO:430). Preferably, hybridization occurs under stringent hybridization and wash conditions.

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In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, more preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same manure polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203323 (DNA75393-1664), or (b) the complement of the DNA molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 203323 (DNA75393-1664).

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In a still further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 80% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity, on the sequence of amino acid residues from about 31 to about 243, inclusive of Figure 246 (SEQ ID NO.431), or the complement of the DNA of (a).

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In a further aspect, the invention concerns an isolated nucleic acid molecule having at least about 50 nucleotides, and preferably at least about 100 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1550 polypeptide having the sequence of amino acid residates from about 31 to about 243, inclusive of Figure 246 (SEQ ID NO-431), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about at 80% sequence identity, preferably at least about at 85% sequence identity, most preferably at least about at 95% sequence identity, most preferably at least about at 95% sequence identity, most preferably at least about at 95% sequence identity to (a) or (b), isolating the test DNA molecule.

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In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1550 polypeptide, with or without the N-terminal signal sequence motion the initiating methionine, or is complementary to such encoding nucleic acid molecule. The signal peptide has been remainvely identified as extending from amino acid position 1 through about amino acid position 30 in the sequence of Figure 246 (SEQ ID NO:431).

In another aspect, the invention concerns an isolated aucheic acid molecule comprising (a) DN/ cacoding a polypeptide scoring at least about 89% positives, preferably at least about 85% positives, more

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preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to about 243, inclusive of Figure 246 (SEQ ID NO:431), or (b) the complement of the DNA of (a).

Another embodiment is directed to fragments of a PRO1550 polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, profectably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 50 nucleotides in length, and most preferably from about 20 to about 40 nucleotides in length.

In another embodiment, the invention provides isolated PRO1530 polypeptide encoded by any of the isolated nucleic acid sequences hereinabove defined.

In another acreer the invention provides isolated native sequence PRO1550 polypeptide, which in our

10 embodiment, includes an amino acid sequence comprising residues 31 to 243 of Figure 246 (SEQ ID NO:431).

In another acreer the invention operators in followed BDD11550 accompany.

In another aspect, the invention concerns an isolated PRO1530 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 90% sequence identity to the sequence of amino acid residues 31 to about 243, inclusive of Figure 246 (SEQ ID NO:431).

15 In a further aspect, the invention concerns an isolated PRO1550 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 31 to 243 of Figure 246 (SEQ ID NO:431).

In yet another aspect, the invention concerns an isolated PRO1550 polypeptide, comprising the sequence
20 of amino acid residues 31 to about 243, inclusive of Figure 246 (SEQ ID NO:431), or a fragment thereof
sufficient to provide a binding site for an anti-PRO1550 antibody. Preferably, the PRO1550 fragment retains
a qualitative biological activity of a native PRO1550 polypeptide.

In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule encoding a PRO1550 polypeptide having the sequence of amino acid residues from about 31 to about 243, inclusive of Figure 246 (SEQ ID NO:431), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80 % sequence identity, professably at least about an 85 % sequence identity, more preferably at least about a 90 % sequence identity, more preferably at least about a 90 % sequence identity or (a) or (b), (ii) culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

24. Additional Embodiments

In other embodiments of the present invention, the invention provides vertors comprising DNA encoding any of the herein described polypeptides. Host cell comprising any such vector are also provided. By 35 way of example, the host cells may be CHO cells, E. coli, or yeast. A process for producing any of the herein described polypeptides is further provided and comprises culturing host cells under conditions suitable for expression of the desired polypeptide and recovering the desired polypeptide from the cell culture.

In other embodiments, the invention provides chimeric molecules comprising any of the herein described polypeprides fused to a heterologous polypepride or amino acid sequence. Example of such chimeric molecules comprise any of the herein described polypeprides fused to an epitope tag sequence or a fe region of an immunoglobulin.

In another embodiment, the invention provides an antibody which specifically binds to any of the above or below described polypeptides. Optionally, the antibody is a monoclonal antibody, humanized antibody antibody fragment or single-chain antibody.

In yet other embodiments, the invention provides oligonucleotide probes useful for isolating genomic and cDNA nucleotide sequences, wherein those probes may be derived from any of the above or below described nucleotide sequences.

10 In other embodiments, the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence that encodes a PKO polypeptide.

З 20 2 domain of a transmembrane protein, with or without the signal peptide, as disclosed herein, or (b) the complement of the DNA molecule of (a). as disclosed herein, an amino acid sequence lacking the signal peptide as disclosed herein or an extracellular more preferably at least about 94% sequence identity, yet more preferably at least about 95% sequence identity, 84% sequence identity, yet more preferably at least about 85% sequence identity, yet more preferably at least yet more preferably at least about 96% sequence identity, yet more preferably at least about 97% sequence at least about 90% sequence identity, yet more preferably at least about 91% sequence identity, yet more sequence identity to (a) a DNA molecule encoding a PRO polypoptide having a full-length amino acid sequence identity, yet more preferably at least about 98% sequence identity and yet more preferably at least about 99% preferably at least about 92% sequence identity, yet more preferably at least about 93% sequence identity, yet least about 88% sequence identity, yet more proferably at least about 89% sequence identity, yet more proferably about 86% sequence identity, yet more preferably at least about 87% sequence identity, yet more preferably at sequence identity, yet more preferably at least about 83 % sequence identity, yet more preferably at least about 80% sequence identity, preferably at least about 81% sequence identity, more preferably at least about 82% In one aspect, the isolated nucleic acid molecule comprises a nucleotide sequence having at least about

In other aspects, the isolated nucleic acid molecule comprises a nucleotide sequence identity, preferably at least about 81% sequence identity, more preferably at least about 82% sequence identity, yet more preferably at least about 81% sequence identity, yet more preferably at least about 84% sequence identity, yet more preferably at least about 85% sequence identity, yet more preferably at least about 85% sequence identity, yet more preferably at least about 85% sequence identity, yet more preferably at least about 85% sequence identity, yet more preferably at least about 85% sequence identity, yet more preferably at least about 85% sequence identity, yet more preferably at least about 91% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 93% sequence identity, yet more preferably at least about 93% sequence identity.

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sequence identity to (a) a DNA molecule comprising the coding sequence of a full-length PRO polypeptide cDNA as disclosed herein, the coding sequence of a PRO polypeptide tacking the signal peptide as disclosed herein or the coding sequence of an extracellular domain of a transmembrane PRO polypeptide, with or without the signal peptide, as disclosed herein, or (b) the complement of the DNA molecule of (a).

5 5 preferably at least about 99% sequence identity to (a) a DNA molecule that encodes the same mature polypeptide at least about 97% sequence identity, yet more preferably at least about 98% sequence identity and yet more 91% sequence identity, yet more preferably at least about 92% sequence identity, yet more preferably at least sequence identity, yet more preferably at least about 90% sequence identity, yet more preferably at least about sequence having at least about 80% sequence identity, preferably at least about 81% sequence identity, more complement of the DNA molecule of (a). encoded by any of the human princin eDNAs deposited with the ATCC as disclosed berein, or (b) the least abour 95 % sequence identity, yet more preferably at least about 96 % sequence identity, yet more preferably abour 93% sequence identity, yet more preferably at least about 94% sequence identity, yet more preferably at idenity, yet more preferably at least about 88% sequence identily, yet more preferably at least about 89% yet more preferably at least about 86% sequence identity, yet more preferably at least about 87% aequence preforably at least about 82% sequence identity, yet more preferably at least about 83% sequence identity, yet more preferably at least about 84% sequence identity, yet more preferably at least about 85% sequence identity In a further aspect, the invention concerns an isolated nucleic acid molecule comprising a nucleotide

Another aspect the invention provides an isolated nucleic acid molecule comprising a nucleotide sequence executing a PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-20 inactivated, or is complementary to such encuding nucleotide sequence, wherein the transmembrane domain(s) of such polypeptide are disclosed herein. Therefore, soluble extracellular domains of the herein described PRO polypeptides are contemplated.

ß 30 23 yet more preferably at least about 190 nucleotides in length, yet more preferably at least about 200 nucleotides nucleotides in length, yet more preferably at least about 350 nucleotides in length, yet more preferably at least in length, yet more preferably at least about 250 nucleotides in length, yet more preferably at least about 300 length, yet more preferably at least about 100 nucleotides in length, yet more preferably at least about 110 encode a polypoptide comprising a binding site for an anti-PRO antibody. Such nucleic acid fragments are preferably at least about 170 nucleotides in length, yet more preferably at least about 180 nucleotides in length at least about 150 nucleorides in length, yet more preferably at least about 160 nucleorides in length, yet more nucleoxides in length, yet more preferably at least about 120 nucleoxides in length, yet more preferably at least preferably at least about 60 nucleotides in leagth, yet more preferably at least about 70 nucleotides in length, yet at least about 40 mucleotides in length, yet more preferably at least about 50 nucleotides in length, yet more usually at least about 20 nucleotides in length, preferably at least about 30 nucleotides in length, more preferably as, for example, hybridization probes or for encoding fragments of a PRO polypeptide that may optionally about 130 nucleotides in length, yet more preferably at least about 140 nucleotides in length, yet more preferably more preferably at least about 80 nucleotides in length, yet more preferably at least about 90 nucleotides in Another embodiment is directed to fragments of a PRO polypeptide coding sequence that may find use

identity, yet more preferably at least about 98% sequence identity and yet more preferably at least about 99%

about 440 nucleotides in length, yet more preferably at least about 450 nucleotides in length, yet more preferably at least about 500 nucleotides in length, yet more preferably at least about 500 nucleotides in length, yet more preferably at least about 500 nucleotides in length, yet more preferably at least about 700 nucleotides in length, yet more preferably at least about 1000 nucleotides in length, yet more preferably at least about 1000 nucleotides in length, yet more preferably at least about 1000 nucleotides in length, wherein in this context the term "about" means the referenced nucleotide sequence length plus or minus 10% of that referenced length. It is noted that novel fragments of a PRO polypeptide-encoding nucleotide sequence with other known nucleotide sequences using any of a number of well known sequence alignment programs and determining which PRO polypeptide-encoding nucleotide sequences are contemplated herein. Also contemplated are the PRO polypeptide fragments encoded by these nucleotide molecule fragments, preferably those PRO polypeptide fragments that comprise a binding site for an anti-PRO amibody.

In another embodiment, the invention provides isolated PRO polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

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ß 20 5 preferably at least about 99% sequence identity to a PRO polypeptide having a full-length amino acid sequence domain of a transmembrane protein, with or without the signal peptide, as disclosed herein. as disclosed herein, an amino acid sequence lucking the signal peptide as disclosed herein or an extracellular at least about 97% sequence identity, yet more preferably at least about 98% sequence identity and yet more sequence identity, yet more preferably at least about 90% sequence identity, yet more preferably at least about about 93% sequence identity, yet more preferably at least about 94% sequence identity, yet more preferably at 91% sequence idenity, yet more preferably at least about 92% sequence identity, yet more preferably at least sequence having at least about 80% sequence identity, preferably at least about 81% sequence identity, more least about 95 % sequence identity, yet more preferably at least about 96 % sequence identity, yet more preferably yet more preferably at least about 86% sequence identity, yet more preferably at least about 87% sequence preferably at least about 82% sequence identity, yet more preferably at least about 83% sequence identity, yet idemity, yet more preferably at least about 88% sequence identity, yet more preferably at least about 89% more preferably at least about 84% sequence identity, yet more preferably at least about 85% sequence identity, In a certain aspect, the invention concerns an isolated PRO polypeptide, comprising an amino acid

In a further aspect, the invertion concerns an isolated PRO polypeptide comprising an amino acid sequence having at least about 81 % sequence identity, more 30 preferably at least about 81 % sequence identity, yet more preferably at least about 83 % sequence identity, yet more preferably at least about 83 % sequence identity, yet more preferably at least about 85 % sequence identity, yet more preferably at least about 85 % sequence identity, yet more preferably at least about 87 % sequence identity, yet more preferably at least about 87 % sequence identity, yet more preferably at least about 89 % sequence identity, yet more preferably at least about 89 % sequence identity, yet more preferably at least about 90 % sequence identity, yet more preferably at least about 91 % sequence identity, yet more preferably at least about 92 % sequence identity, yet more preferably at least about 93 % sequence identity, yet more preferably at least about 94 % sequence identity, yet more preferably at least about 94 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity, yet more preferably at least about 95 % sequence identity yet more preferably at least about 95 % sequence identity yet more

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at least about 97% sequence identity, yet more preferably at least about 98% sequence identity and yet more preferably at least about 99% sequence identity to an amino acid sequence encoded by any of the human protein cDNAs deposited with the ATCC as disclused herein.

In a further aspect, the invention concerns an isolated PRO polypeptide comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 81% positives, preferably at least about 81% positives, per more preferably at least about 83% positives, yet more preferably at least about 83% positives, yet more preferably at least about 85% positives, yet more preferably at least about 95% positives, yet more preferably

In a specific sepect, the invention provides an isolated PRO polypeptide without the N-terminal signal sequence and/or the initiating methirmine and is encoded by a muclostide sequence that encodes such an amino anid sequence as hereimbefore described. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the appropriate encoding medicic acid molecule under coordinators suitable for expression of the PRO polypeptide and recovering the PRO

20 nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

Another aspect the invention provides an isolated PRO polypeptide which is either transmembrane domain-deleted or transmembrane domain-inactivated. Processes for producing the same are also herein described, wherein those processes comprise culturing a host cell comprising a vector which comprises the 25 appropriate exceeding nucleic acid molecule under conditions suitable for expression of the PRO polypeptide and recovering the PRO polypeptide from the cell culture.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO polypeptide as defined berein. In a particular embodiment, the agonist or antagonist is an anti-PRO antibody or a small molecule.

30 In a further embodiment, the invention concerns a method of identifying agentius or assignments to a PRO polypeptide which comprise contacting the PRO polypeptide with a candidate molecule and monitoring a biological activity mediated by said PRO polypeptide. Preferably, the PRO polypeptide is a native PRO polypeptide.

In a still further embodiment, the invention concerns a composition of matter comprising a PRO 35 polypeptide, or an agonist or antagonist of a PRO polypeptide as herein described, or an anti-PRO antibody, in combination with a carrier. Optionally, the currier is a pharmaccutically acceptable carrier.

Another embodiment of the present invention is directed to the use of a PRO polypeptide, or an agonis

or aniagonist thereof as hereinbefore described, or an anti-PRO antibody, for the preparation of a medicamen useful in the treatment of a condition which is responsive to the PRO polypeptide, an agonist or antagonist thereof or an anti-PRO antibody.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows a nucleotide sequence (SEQ ID NO:3) of a native sequence PRO1560 (UNQ767) cDNA, wherein SEQ ID NO:3 is a clone designated herein as "DNA19902-1669". The start and stop codons are shown in bold and underlined form.

Figure 2 shows the amino acid scquence (SEQ ID NO:4) derived from the coding sequence of SEQ ID NO:3 shown in Figure 1.

10 Figure 3 shows a nucleotide sequence (SEQ ID NO.5) of a native sequence PRO444 (UNQ328) cDNA, wherein SEQ ID NO:5 is a clone designated herein as "DNA26846-1397". The start and stop codons are shown in bold and underlined font.

Figure 4 shows the amino acid sequence (SEQ ID NO:6) derived from the coding sequence of SEQ ID NO:5 shown in Figure 3.

15 Figure 5 shows a nucleotide sequence (SEQ ID NO:7) of a native sequence PRO1018 (UNQS01) cDNA, wherein SEQ ID NO:7 is a clone designated herein as "DNA56107-1415". The start and stop codons are shown in bold and underlined font.

Figure 6 shows the amino acid sequence (SEQ ID NO:8) derived from the coding sequence of SEQ ID NO:7 shown in Figure 5.

20 Figure 7 shows a nucleotide sequence (SEQ ID NO:9) of a native sequence PRO1773 (UNQ835) cDNA, wherein SEQ ID NO:9 is a clone designated herein as "DNA56406-1704". The start and stop codons are shown in boild and underlined font.

Figure 8 shows the amino acid sequence (SEQ ID NO:10) derived from the coding sequence of SEQ ID NO:9 shown in Figure 7.

25 Figure 9 shows a nucleotide sequence (SEQ ID NO:11) of a native sequence PRO1477 (UNQ747) cDNA, wherein SEQ ID NO:11 is a clone designated herein as "DNA56529-1647". The start and stop codons are shown in boild and underlined from.

Figure 10 shows the amino acid sequence (SEQ ID NO:12) derived from the coding sequence of SEQ ID NO:11 shown in Figure 9.

Figure 11 shows a mucleotide sequence (SEQ ID NO:16) of a native sequence PRO1478 (UNQ748) cDNA, wherein SEQ ID NO:16 is a clone designated herein as "DNA56531-1648". The start and stop codons are shown in bold and underlined form.

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Figure 12 shows the unino acid sequence (SEQ ID NO:17) derived from the coding sequence of SEQ ID NO:16 shown in Figure 11.

35 Figure 13 shows a nucleoible sequence (SEQ ID NO.21) of a naive sequence PRO831 (UNQ47), cDNA, wherein SEQ ID NO.21 is a clone designated herein as "DNA56862-1343". The start and stop codons are shown in bold and underlined fout.

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Figure 14 shows the amino acid sequence (SEQ ID NO:22) derived from the coding sequence of SEQ ID NO:21 shown in Figure 13.

Figure 13 shows a nucleotide sequence (SEQ ID NO:23) of a nutive sequence PRO1113 (UNQ556) cDNA, wherein SEQ ID NO:23 is a clone designated herein as "DNA57254-1477". The sunt and stop codons are shown in bold and underlined font.

Figure 16 shows the smino acid sequence (SEQ ID NO:24) derived from the coding sequence of SEQ ID NO:23 shown in Figure 15.

Figure 17 shows a nucleotide sequence (SEQ ID NO:28) of a native sequence PRO1194 (UNQ607) cDNA, wherein SEQ ID NO:28 is a clone designated herein as "DNA57841-1522". The start and stop codons are shown in bold and underlined font.

10 Figure 18 shows the amino acid sequence (SEQ ID NO.29) derived from the coding sequence of SEQ ID NO.28 shown in Figure 17.

Figure 19 shows a nucleotide sequence (SEQ ID NO:30) of a native sequence PRO1110 (UNQ553) cDNA, wherein SEQ ID NO:30 is a clone designated herein as *DNA58727-1474*. The start and stop codors are shown in bold and underlined font.

15 Figure 20 shows the amino acid sequence (SEQ ID NO.31) derived from the coding sequence of SEQ ID NO.30 shown in Figure 19.

Figure 21 shows a nucleotide sequence (SEQ ID NO.32) of a native sequence PRO1378 (UNQ715) cDNA, wherein SEQ ID NO.32 is a clone designated herein as *DNAS8730-1607*. The start and stop codons are shown in bold and underlined from

20 Figure 22 shows the amino acid sequence (SEQ ID NO.33) derived from the coding sequence of SEQ ID NO.32 shown in Figure 21.

Figure 23 shows a nucleotide sequence (SEQ ID NO:40) of a narive sequence PRO1481 (UNQ750) cDNA, wherein SEQ ID NO:40 is a clone designated herein as "DNA58732-1650". The start and stop codons are shown in bold and underlined font.

25 Figure 24 shows the amino acid sequence (SEQ ID NO:41) derived from the coding sequence of SEO ID NO:40 shown in Figure 23.

Figure 25 shows a nucleotide sequence (SEQ ID NO:42) of a native sequence PRO1189 (UNQ603) cDNA, wherein SEQ ID NO:42 is a clone designated herein as "DNA58828-1519". The start and stop codots are shown in bold and underlined font.

30 Figure 26 shows the amino acid sequence (SEQ ID NO:43) derived from the coding sequence of SEQ ID NO:42 shown in Figure 25.

Figure 27 shows a nucleotide sequence (SEQ ID NO:49) of a native sequence PRO1415 (UNQ731); cDNA, wherein SEQ ID NO:49 is a clone designated herein as "DNA58852-1637". The start and stop codons are shown in bold and underlined from.

35 Figure 28 shows the amino acid sequence (SEQ ID NO:50) derived from the coding sequence of SEQ ID NO:49 shown in Figure 27.

Figure 29 shows a nucleotide sequence (SEQ ID NO:51) of a native sequence PRO1411 (UNQ729) cDNA, wherein SEQ ID NO:51 is a clone designated herein as "DNA59212-1627". The start and stop codons are shown in bold and underlined font.

Figure 30 shows the amino acid sequence (SEQ ID NO:52) derived from the coding sequence of SEQ NO:51 shown in Figure 29.

Figure 31 shows a nucleoside sequence (SEQ ID NO:53) of a native sequence PRO1295 (UNQ664) cDNA, wherein SEQ ID NO:53 is a clone designated herein as "DNA59218-1559". The start and stop codons are shown in bold and underlined font.

Figure 32 shows the amino acid sequence (SEQ ID NO:54) derived from the coding sequence of SEQ ID NO:53 shown in Figure 31.

10 Figure 33 shows a nucleotide sequence (SEQ ID NO:55) of a native sequence PRO1359 (UNQ708) cDNA, wherein SEQ ID NO:55 is a clone designated herein as "DNA59219-1613". The start and stop codons are shown in bold and underlined form.

Figure 34 shows the amino acid sequence (SEQ ID NO:56) derived from the coding sequence of SEQ ID NO:55 shown in Figure 33.

Figure 35 shows a nucleotide sequence (SEQ ID NO:57) of a native sequence PRO1190 (UNQ604) cDNA, wherein SEQ ID NO:57 is a clone designated herein as "DNA59586-1520". The start and stop codons are shown in bold and underlined (om.

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Figure 36 shows the amino acid sequence (SEQ ID NO:58) derived from the coding sequence of SEQ ID NO:57 shown in Figure 35.

20 Figure 37 shows a nucleotide sequence (SEQ ID NO:62) of a native sequence PRO1772 (UNQ834) cDNA, wherein SEQ ID NO:62 is a clone designated herein as "DNA59817-1703". The start and stop codons are shown in bold and underlined font.

Figure 38 shows the amino acid sequence (SEQ ID NO.63) derived from the coding sequence of SEQ ID NO.62 shown in Figure 37.

25 Figure 39 shows a nucleotide sequence (SEQ ID NO:67) of a native sequence PRO1248 (IJNQ631) cDNA, wherein SEQ ID NO:67 is a clone designated herein as "DNA60278-1530". The start and stop codons are shown in bold and underlined funt.

Figure 40 abows the amino acid sequence (SEQ ID NO:68) derived from the coding sequence of SEQ ID NO:67 abown in Figure 39.

30 Figure 41 shows a nucleotide sequence (SEQ ID NO:69) of a native sequence PRO1316 (UNQ682) cDNA, wherein SEQ ID NO:69 is a clone designated herein as "DNA60608-1577". The start and stop codons are shown in bold and underlined front.

Figure 42 shows the amino acid sequence (SEQ ID NO:70) derived from the coding sequence of SEQ ID NO:69 shown in Figure 41.

35 Figure 43 shows a nucleotide sequence (SEQ ID NO:71) of a native sequence PRO1197 (UNQ610) cDNA, wherein SEQ ID NO:71 is a clone designated herein as "DNA60611-1524". The start and stop codons are shown in bold and underlined form.

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Figure 44 shows the amino acid sequence (SEQ ID NO:72) derived from the coding sequence of SEQ ID NO:71 shown in Figure 43.

Figure 45 shows a nucleotide sequence (SEQ ID NO:76) of a native sequence PRO1293 (UNQ662) cDNA, wherein SEQ ID NO:76 is a clone designated herein as "DNA60618-1557". The start and stop codous are shown in bold and underlined form.

Figure 46 shows the amino acid sequence (SEQ ID NO:77) derived from the coding sequence of SEQ ID NO:76 shown in Figure 45.

Figure 47 shows a nucleotide sequence (SEQ ID NO:78) of a native sequence PRO1380 (UNQ717) cDNA, wherein SEQ ID NO:78 is a clone designated herein as "DNA60740-1615". The start and stop codons are shown in bold and underlined font.

Figure 48 shows the amino acid sequence (SEQ ID NO:79) derived from the coding sequence of SEQ ID NO:78 shown in Figure 47.

Figure 49 shows a nucleotide sequence (SEQ ID NO:83) of a maive sequence PRO1265 (UNQ636) cDNA, wherein SEQ ID NO:83 is a clone designated herein as "DNA60764-1533". The start and stop codons are shown in bold and underlined four.

15 Figure 50 shows the amino acid sequence (SEQ ID NO:84) derived from the coding sequence of SEQ ID NO:83 shown in Figure 49.

Figure 51 shows a nucleotide sequence (SEQ ID NO:85) of a native sequence PRO1250 (UNQ633) cDNA, wherein SEQ ID NO:85 is a clone designated herein as "DNA60775-1532". The start and stop codons are shown in bold and underlined font.

20 Figure 52 shows the amino acid sequence (SEQ ID NO:86) derived from the coding sequence of SEQ ID NO:85 shown in Figure 51.

Figure 53 shows a nucleotide sequence (SEQ ID NO:87) of a native sequence PRO1475 (INQ746) cDNA, wherein SEQ ID NO:87 is a clone designated herein as "DNA61185-1646". The start and stop codons are shown in bold and underlined font.

Figure 54 shows the amino acid sequence (SEQ ID NO:88) derived from the coding sequence of SEQ ID NO:87 shown in Figure 53.

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Figure 55 shows a nucleotide sequence (SEQ ID NO:94) of a native sequence PRO1377 (UNQ714) cDNA, wherein SEQ ID NO:94 is a clone designated herein as "DNA61608-1606". The start and stop codons are shown in bold and underlined font.

30 Figure 56 shows the amino acid sequence (SEQ ID NO:95) derived from the coding sequence of SEQ ID NO:94 shown in Figure 55.

Figure 57 shows a nucleotide sequence (SEQ ID NO:99) of a native sequence PRO1326 (UNQ886) cDNA, wherein SEQ ID NO:99 is a clone designated herein as "DNA62808-1582". The start and stop codons are shown in bold and underlined font.

Figure 58 shows the amino acid sequence (SEQ ID NO:100) derived from the coding sequence of SEQ ID NO:99 shown in Figure 57.

Figure 59 shows a nucleotide sequence (SEQ ID NO:101) of a native sequence PRO1249 (I)NQ632) cDNA, wherein SEQ ID NO:101 is a clone designated herein as "DNA62809-1531". The start and stop codons are shown in bold and underlined font.

Figure 60 shows the amino acid sequence (SEQ ID NO:102) derived from the coding sequence of SEQ D NO:100 shown in Figure 59.

Figure 61 shows a nucleotide sequence (SEQ ID NO:103) of a native sequence PRO1315 (UNQ681) cDNA, wherein SEQ ID NO:103 is a clone designated herein as "DNA62815-1578". The start and stop codots are shown in bold and underlined font.

Figure 62 shows the amino acid sequence (SEQ ID NO:104) derived from the coding sequence of SEQ ID NO:103 shown in Figure 61.

10 Figure 63 shows a nucleotide sequence (SEQ ID NO:110) of a native sequence PRO1549 (DNQ782) cDNA, wherein SEQ ID NO:110 is a clone designated herein as "DNA62845-1684". The start and stop codous are shown in bold and underlined font.

Figure 64 shows the amino acid sequence (SEQ ID NO:111) derived from the coding sequence of SEQ ID NO:110 shown in Figure 63.

Figure 65 shows a nucleotide sequence (SEQ ID NO:115) of a native sequence PRO1430 (UNQ736) cDNA, wherein SEQ ID NO:115 is a clone designated herein as "DNA64842-1632". The start and stop codons are shown in bold and underlined four.

Figure 66 shows the amino acid sequence (SEQ ID NO:116) derived from the coding sequence of SEQ ID NO:115 shown in Figure 65.

Figure 67 shows a nucleotide sequence (SEQ ID NO:117) of a native sequence PRO1374 (UNQ711) cDNA, wherein SEQ ID NO:117 is a clone designated herein as "DNA64849-1604". The start and stop codons are shown in bold and underlined font.

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Figure 68 shows the amino acid sequence (SEQ ID NO:118) derived from the coding sequence of SEQ ID NO:117 shown in Figure 67.

Figure 69 shows a nucleotide scaperace (SEQ ID NO:122) of a native sequence PRO1311 (UNQ677) cDNA, wherein SEQ ID NO:122 is a clone designated herein as *DNA64863-1573*. The start and stop codous are shown in bold and underlined font.

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Figure 70 shows the amino acid sequence (SEQ ID NO:123) derived from the coding sequence of SEQ ID NO:122 shown in Figure 69.

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Figure 71 shows a nucleotide sequence (SEQ ID NO:127) of a native sequence PRO1357 (UNQ706) cDNA, wherein SEQ ID NO:127 is a clone designated herein as "DNA64881-1602". The start and stop codons are shown in bold and underlined forst.

Figure 72 shows the amino acid sequence (SEQID NO:128) derived from the coding sequence of SEQID NO:127 shown in Figure 71.

Figure 73 shows a nucleotide sequence (SEQ ID NO:129) of a native sequence PRO1244 (UNQ628) cDNA, wherein SEQ ID NO:129 is a clone designated herein as *DNA64883-1326*. The start and stop codons are shown in bold and underlined four.

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Figure 74 shows the amino acid sequence (SEQ ID NO:130) derived from the coding sequence of SEQ ID NO:129 shown in Figure 73.

Figure 75 shows a nucleotide sequence (SEQ ID NO:131) of a native sequence PRO1246 (UNQ630) cDNA, wherein SEQ ID NO:131 is a clone designated herein as "DNA64885-3529". The start and stop codons are shown in bold and underlined form.

Figure 76 shows the amino acid sequence (SEQ ID NO:132) derived from the coding sequence of SEQ ID NO:131 shown in Figure 75.

Figure 77 shows a nucleotide sequence (SEQ ID NO:133) of a narive sequence PRO(356 (UNQ705) cDNA, wherein SEQ ID NO:133 is a clone designated herein as *DNA64886-1601.* The start and stop codons are shown in bold and underlined font.

Figure 78 shows the amino acid sequence (SEQ ID NO:134) derived from the coding sequence of SEQ ID NO:133 shown in Figure 77.

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Figure 79 shows a nucleotide sequence (SEQ ID NO:135) of a naive sequence PRO1275 (INQ645) cDNA, wherein SEQ ID NO:135 is a clone designated herein as "DNA64888-1542". The start and stop codons are shown in bold and underlined font.

Figure 80 shows the anino acid sequence (SEQ ID NO:136) derived from the coding sequence of SEQ ID NO:135 shown in Figure 79.

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Figure 81 shows a nucleotide sequence (SEQ ID NO:137) of a native sequence PRO1274 (UNQ644) cDNA, wherein SEQ ID NO:137 is a close designated herein as "DNA64889-1542". The start and stop codons are shown in bold and underlined font.

20 Figure 82 shows the amino acid sequence (SEQ ID NO:138) derived from the coding sequence of SEQ ID NO:137 shown in Figure 81.

Figure 83 shows a nucleotide sequence (SEQ ID NO:139) of a native sequence PRO1412 (UNQ730) cDNA, wherein SEQ ID NO:139 is a clone designated herein as "DNA64897-1628". The start and stop codons are shown in bold and underlined form.

25 Figure 84 shows the amino acid sequence (SEQ ID NO: 140) derived from the coding sequence of SEQ ID NO: 139 shown in Figure 83.

Figure 85 shows a nucleoside sequence (SEQ ID NO:141) of a native sequence PRO1557 (UNQ765) cDNA, wherein SEQ ID NO:141 is a close designated herein as "DNA64902-1667". The start and stop colons are shown in bold and underlined fort.

30 Figure 86 shows the amino acid sequence (SEQ ID NO:142) derived from the coding sequence of SEQ ID NO:141 shown in Figure 85.

Figure 87 shows a nucleotide sequence (SEQ ID NO:143) of a native sequence PRO1286 (UNQ655) cDNA, wherein SEQ ID NO:143 is a clone designated herein as "DNA64903-1553". The start and stop codons are shown in bold and underlined font.

35 Figure 88 shows the amino acid sequence (SEQ ID NO:144) derived from the coding sequence of SEQ ID NO:143 shown in Figure 87.

cDNA, wherein SEQ ID NO: 145 is a clone designated herein as "DNA64905-1558". The start and stop codons Figure 89 shows a nucleotide sequence (SEQ ID NO:145) of a native sequence PRO1294 (UNQ663)

Figure 90 shows the amino acid sequence (SEQ ID NO:146) derived from the coding sequence of SEQ

cDNA, wherein SEQ ID NO:147 is a clone designated herein as "DNA64950-1590". The start and stop codons are shown in bold and underlined font. Figure 91 shows a muckotide sequence (SEQ ID NO:147) of a native sequence PRO1347 (UNQ702)

Figure 92 shows the amino acid sequence (SEQ ID NO:148) derived from the coding sequence of SEQ

ö cDNA, wherein SEQ ID NO: 152 is a clone designated herein as "DNA64952-1568". The start and stop codons Figure 93 shows a nucleotide sequence (SEQ ID NO:152) of a native sequence PRO1305 (UNQ671)

Figure 94 shows the amino acid sequence (SEQ ID NO:153) derived from the coding sequence of SEC

ï are shown in bold and underlined font. cDNA, wherein SEQ ID NO:157 is a clone designated herein as "DNA65402-1540". The start and stop codons Figure 95 shows a nucleotide sequence (SEQ ID NO:157) of a native sequence PRO1273 (UNQ643)

ID NO:157 shown in Figure 95. Figure 96 shows the amino acid sequence (SEQ ID NO:158) derived from the coding sequence of SEQ

cDNA, wherein SEQ ID NO: 159 is a clone designated herein as "DNA65403-1565". The start and stop codons are shown in bold and underlined font. Figure 97 shows a nucleotide sequence (SBQ ID NO:159) of a native sequence PRO1302 (UNQ668)

ID NO:159 shown in Figure 97. Figure 98 shows the amino acid sequence (SEQ ID NO:160) derived from the coding sequence of SEQ

25 cDNA, wherein SEQ ID NO:161 is a clone designated herein as "DNA65404-1551". The start and stop codons are shown in bold and underlined font Figure 99 shows a nucleotide sequence (SEQ ID NO:161) of a native sequence PRO1283 (UNQ653)

ID NO:161 shown in Figure 99. Figure 100 shows the amino acid sequence (SEQ ID NO:162) derived from the coding sequence of SEQ

cDNA, wherein SEQ ID NO:169 is a clone designated herein as "DNA65405-1547". The start and stop codons are shown in bold and underlined form. Figure 101 shows a nucleotide sequence (SEQ ID NO: 169) of a native sequence PRO1279 (UNQ649)

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ID NO:169 shown in Figure 101. Figure 102 shows the amino acid sequence (SEQ ID NO:170) derived from the coding sequence of SEQ

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cDNA, wherein SEQID NO:179 is a clone designated herein as "DNA65406-1567". The start and stop codons are shown in bold and underlined font Figure 103 shows a mucleotide sequence (SEQ ID NO:179) of a native sequence PRO1304 (UNQ670)

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ID NO:179 shown in Figure 103. Figure 104 shows the amino acid sequence (SEQ ID NO:180) derived from the coding sequence of SEQ

cDNA, wherein SEQ ID NO: 188 is a clone designated herein as "DNA65408-1578". The start and stop codons Figure 105 shows a nucleotide sequence (SEQ ID NO:188) of a native sequence PRO1317 (UNQ683)

ID NO:188 shown in Figure 105. Figure 106 shows the amino acid sequence (SEQ ID NO:189) derived from the coding sequence of SEQ

are shown in bold and underlined font. cDNA, wherein SEQ ID NO: 193 is a clone designated herein as "DNA65409-1566". The start and stop codons Figure 107 shows a nucleoride sequence (SEQ ID NO:193) of a native sequence PRO1303 (UNQ669)

tD NO:193 shown in Figure 107. Figure 108 shows the amino acid sequence (SEQ ID NO:194) derived from the coding sequence of SEQ

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are shown in bold and underlined font. cDNA, wherein SEQID NO:195 is a clone designated herein as "DNA65410-1569". The start and stop codons Figure 109 shows a nucleotide sequence (SEQ ID NO:195) of a native sequence PRO 1306 (UNQ 672)

ID NO:195 shown in Figure 109. Figure 110 shows the amino acid sequence (SEQ ID NO: 196) derived from the coding sequence of SEQ

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stop codons are shown in bold and underlined font. (UNQ691) cDNA, wherein SEQ ID NO: 197 is a clone designated herein as "DNA65423-1595". The start and Figures 111A-B show a nucleotide sequence (SEQ ID NO:197) of a native sequence PRO1336

20 ID NO:198 shown in Figures 111A-B. Figure 112 shows the amino acid sequence (SEQ ID NO: 198) derived from the coding sequence of SEQ

are shown in bold and underlined font. cDNA, wherein SEQ ID NO:202 is a clone designated herein as "DNA66304-1346". The start and stop codons Figure 113 shows a nucleotide sequence (SEQ ID NO:202) of a native sequence PRO1278 (UNQ648)

z ID NO:202 shown in Figure 113. Figure 114 shows the amino acid sequence (SEQ ID NO:203) derived from the coding sequence of SEQ

cDNA, wherein SEQ ID NO:209 is a clone designated herein as "DNA66511-1563". The start and stop codons are shown in bold and underlined font. Figure 115 shows a nucleotide sequence (SEQ ID NO:209) of a native sequence PRO1298 (UNQ666)

30 ID NO:209 shown in Figure 115 Figure 116 shows the amino acid sequence (SEQ ID NO:210) derived from the coding sequence of SEQ

cDNA, wherein SEQID NO:211 is a clone designated herein as "DNA66512-1564". The start and trop codots are shown in bold and underlined font. Figure 117 shows a nucleotide sequence (SEQ ID NO:211) of a native sequence PRO1301 (UNQ667)

υ ID NO:211 shown in Figure 117. Figure 118 shows the amino suid sequence (SEQ ID NO:212) derived from the coding sequence of SEQ

Figure 119 shows a nucleotide sequence (SEQ ID NO:213) of a native sequence PRO1268 (UNQ638) cDNA, wherein SEQ ID NO:213 is a clone designated herein as "DNA66519-1535". The start and stop codous are shown in bold and underlined font.

Figure 120 shows the amino acid sequence (SEQ ID NO:214) derived from the coding sequence of SEQ D NO:213 shown in Figure 119.

Figure 121 shows a nucleotide sequence (SEQ ID NO:215) of a native sequence PRO1269 (UNQ639) cDNA, wherein SEQ ID NO:215 is a cloue designated herein as "DNA66520-1536". The start and stop codons are shown in bold and underlined four.

Figure 122 shows the amino acid sequence (SEQ ID NO:216) derived from the coding sequence of SEQ ID NO:215 shown in Figure 121.

Figure 123 shows a nucleotide sequence (SEQ ID NO:217) of a native sequence PRO1327 (UNQ687) cDNA, wherein SEQ ID NO:217 is a clone designated herein as "DNA66521-1383". The start and stop codons are shown in hold and underlined font.

Figure 124 shows the amino acid sequence (SEQ ID NO:218) derived from the coding sequence of SEQ ID NO:217 shown in Figure 123.

15 Figure 125 shows a nucleoside sequence (SEQ ID NO:219) of a native sequence PRO1382 (UNQ718) cDNA, wherein SEQ ID NO:219 is a clone designated herein as "DNA66526-1616". The start and stop codons are shown in bold and underlined four.

Figure 126 shows the amino sold sequence (SEQ ID NO.220) derived from the coding sequence of SEQ ID NO.219 shown in Figure 125.

20 Figure 127 shows a nucleotide sequence (SEQ ID NO:224) of a native sequence PRO1328 (UNQ688) cDNA, wherein SEQ ID NO:224 is a clone designated herein as *DNA66658-1584*. The start and stop codons are shown in bold and underlined font.

Figure 128 shows the amino sold sequence (SEQ ID NO:225) derived from the coding sequence of SEQ ID NO:224 shown in Figure 127.

25 Figure 129 shows a nucleoside sequence (SEQ ID NO:226) of a native sequence PRO1325 (UNQ685) cDNA, wherein SEQ ID NO:226 is a clone designated herein as "DNA66659-1593". The start and stop codons are shown in bold and underlined font.

Figure 130 shows the amino acid sequence (SEQ ID NO:227) derived from the coding sequence of SEQ ID NO:226 shown in Figure 129.

Figure 131 shows a nucleotide sequence (SEQ ID NO:228) of a narive sequence PRO1340 (UNQ695) cDNA, wherein SEQ ID NO:228 is a clone designated herein as "DNA66663-1598". The start and stop codons are shown in bold and underlined font.

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Figure 132 shows the amino acid sequence (SEQ ID NO:229) derived from the coding sequence of SEQ ID NO:228 shown in Figure 131.

35 Figure 133 shows a nucleotide sequence (SEQ ID NO:233) of a native sequence PRO1339 (INQ694) cDNA, wherein SEQ ID NO:233 is a clone designated herein as "DNA66669-1597". The start and stop codons are shown in bold and underlined form.

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Figure 134 shows the amino acid sequence (SEQ ID NO:234) derived from the coding sequence of SEQ ID NO:233 shown in Figure 133.

Figure 135 shows a nucleoxide sequence (SEQ ID NO:235) of a narive sequence PRO1337 (UNQ692) cDNA, wherein SEQ ID NO:235 is a cloue designated herein as "DNA66672-1586". The start and stop codons are shown in bold and underlined font.

Figure 136 shows the amino acid sequence (SEQID NO:236) derived from the coding sequence of SEQID NO:235 shown in Figure 135.

Figure 137 shows a nucleotide sequence (SEQ ID NO:242) of a native sequence PRO1342 (UNQ697) cDNA, whertin SEQ ID NO:242 is a clone designated herein as "DNA66674-1599". The start and stop codons are shown in bold and underlined font.

Figure 138 shows the amino acid sequence (SEQ ID NO:243) derived from the coding sequence of SEQ ID NO:242 shown in Figure 137.

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Figure 139 shows a nucleotide sequence (SEQ ID NO:247) of a native sequence PRO1343 (UNQ\$98) cDNA, wherein SEQ ID NO:247 is a clone designated herein as "DNA66675-1587". The start and stop codots are shown in bold and underlined font.

15 Figure 140 shows the amino acid sequence (SEQ ID NO:248) derived from the coding sequence of SEQ ID NO:247 shown in Figure 139.

Figure 141 shown a nucleotide sequence (SEQ ID NO:252) of a native sequence PRO1480 (UNQ749) cDNA, wherein SEQ ID NO:252 is a clone designated herein as "DNA67962-1649". The start and stop codons are shown in bold and underlined font.

20 Figure 142 shows the amino acid sequence (SEQ ID NO:253) derived from the coding sequence of SEQ ID NO:252 shown in Figure 141.

Figures 143A-B show a nucleotide sequence (SEQ ID NO:259) of a native sequence PRO1487 (UNQ756) cDNA, wherein SEQ ID NO:259 is a clone designated herein as *DNA6836-1656*. The start and stop codons are shown in bold and underlined form.

25 Figure 144 shows the amino acid sequence (SEQ ID NO:260) derived from the coding sequence of SEQ ID NO:259 shown in Figures 143A-B.

Figure 145 shows a nucleotide sequence (SEQ ID NO:264) of a native sequence PRO1418 (UNQ732) cDNA, wherein SEQ ID NO:264 is a clone designated herein as *DNA68864-1629*. The start and stop codors are shown in bold and underlined font.

30 Figure 146 shows the amino soid sequence (SEQ ID NO:265) derived from the coding sequence of SEQ ID NO:264 shown in Figure 145.

Figure 147 shows a nucleotide sequence (SEQ ID NO:266) of a native sequence PRO1472 (INQ744) cDNA, wherein SEQ ID NO:266 is a clone designated herein as "DNA68866-1644". The start and stop codons are shown in bold and underlined font.

35 Figure 148 shows the amino acid sequence (SEQ ID NO:267) derived from the coding sequence of SEQ ID NO:265 shown in Figure 147.

Figure 149 shows a nucleotide sequence (SEQ ID NO:268) of a native sequence PRO1461 (UNQ742) cDNA, wherein SEQ ID NO:268 is a clone designated herein as "DNA68871-1638". The start and stop codons are shown in bold and underlined font.

Figure 150 abows the amino acid sequence (SEQ ID NO:269) derived from the coding sequence of SEQ D NO:268 shown in Figure 149.

Figure 151 shows a nucleotide sequence (SEQ ID NO:270) of a native sequence PRO1410 (UNQ728) cDNA, wherein SEQ ID NO:270 is a clone designated herein as "DNA68874-1622". The start and stop codors are shown in bold and underlined form.

Figure 132 shows the amino acid sequence (SEQ ID NO:271) derived from the coding sequence of SEQ ID NO:270 shown in Figure 151.

Figure 153 shows a nucleotide sequence (SEQ ID NO:272) of a native sequence PRO1568 (UNQ774) cDNA, wherein SEQ ID NO:272 is a clone designated herein as *DNA68880-1676*. The start and stop codons are shown in bold and underlined foul.

Figure 154 shows the amino acid sequence (SEQ ID NO:273) derived from the coding sequence of SEQ ID NO:272 abown in Figure 153.

15 Figure 155 shows a nucleotide sequence (SEQ ID NO:274) of a native sequence PRO1570 (UNQ776) cDNA, wherein SEQ ID NO:274 is a clone designated herein as "DNA68885-1678". The start and stop codons are shown in bold and underlined font.

Figure 156 shows the amino acid sequence (SEQ ID NO:275) derived from the coding sequence of SEQ ID NO:274 shown in Figure 155.

20 Figure 157 shows a mucleoride sequence (SEQ ID NO:276) of a native sequence PRO1317 (UNQ783) cDNA, wherein SEQ ID NO:276 is a clone designated herein as "DNA71166-1683". The start and stop codons are shown in bold and underlined font.

Figure 158 shows the amino acid sequence (SEQ ID NO:277) derived from the coding sequence of SEQ ID NO:276 shown in Figure 157.

25 Figure 159 shows a nucleotide sequence (SEQ ID NO:281) of a native sequence PRO1780 (UNQ842) cDNA, wherein SEQ ID NO:281 is a close designated herein as "DNA71169-1709". The start and stop codous are shown in bold and underlined font.

Figure 160 shows the amino acid sequence (SEQ ID NO:282) derived from the coding sequence of SEQ ID NO:281 shown in Figure 159.

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Figure 161 shows a nucleotide sequence (SEQ ID NO:286) of a native sequence PRO1486 (UNQ755) cDNA, wherein SEQ ID NO:286 is a clone designated herein as "DNA71180-1655". The start and stop codons are shown in bold and underlined four.

Figure 162 shows the amino acid sequence (SEQ ID NO:287) derived from the coding sequence of SEQ ID NO:286 shown in Figure 161.

35 Figure 163 shows a nucleotide scrivence (SEQ ID NO:291) of a native sequence PRO1433 (UNQ738) cDNA, wherein SEQ ID NO:291 is a clone designated herein as "DNA71184-1634". The start and stop codons are shown in bold and underlined font.

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Figure 164 shows the amino acid sequence (SEQ ID NO:292) derived from the coding sequence of SEQ D NO:291 shown in Figure 163.

Figure 165 shows a nucleotide sequence (SEQ ID NO.296) of a naive sequence PRO1490 (UNQ759) cDNA, wherein SEQ ID NO.296 is a clone designated herein as "DNA71213-1659". The sunt and stop codons are shown in bold and underlined four.

Figure 166 shows the amino acid sequence (SEQ ID NO:297) derived from the coding sequence of SEQ ID NO:296 shown in Figure 165.

Figure 167 shows a nucleotide sequence (SEQ ID NO:301) of a native sequence PRO1482 (UNQ751) cDNA, wherein SEQ ID NO:301 is a clone designated herein as "DNA71234-1651". The start and stop codors are shown in bold and underlined form.

10 Figure 168 shows the amino acid sequence (SEQ ID NO:302) derived from the coding sequence of SEQ ID NO:301 shown in Figure 167.

Figure 169 shows a nucleotide sequence (SEQ ID NO:303) of a native sequence PRO1446 (UNQ740) cDNA, wherein SEQ ID NO:303 is a clone designated herein as "DNA71277-1636". The start and stop codons are shown in hold and underlined font.

15 Figure 170 shows the amino acid sequence (SEQ ID NO:304) derived from the coding sequence of SEQ ID NO:303 shown in Figure 169.

Figure 171 shows a nucleotide sequence (SEQ ID NO:305) of a native sequence PRO1558 (UNQ766) cDNA, wherein SEQ ID NO:305 is a clear designated herein as *DNA71282-1668*. The start and stop codons are shown in bold and underlined font.

20 Figure 172 shows the amino acid sequence (SEQ ID NO:306) derived from the coding sequence of SEQ ID NO:305 shown in Figure 171.

Figure 173 shows a nucleotide sequence (SEQ ID NO:307) of a native sequence PRO1604 (UNQ785) cDNA, wherein SEQ ID NO:307 is a close designated herein as "DNA71286-1687". The start and stop codons are shown in bold and underlined form.

25 Figure 174 shows the amino acid sequence (SEQ ID NO:308) derived from the coding sequence of SEQ ID NO:307 shown in Figure 173.

Figure 175 shows a nucleotide sequence (SEQ ID NO:309) of a native sequence PRO1491 (UNQ760) cDNA, wherein SEQ ID NO:309 is a close designated herein as *DNA71883-1660*. The start and stop codons are shown in bold and underlined fom.

30 Figure 176 shows the amino acid sequence (SEQ ID NO.310) derived from the coding sequence of SEQ ID NO.309 shown in Figure 175.

Figure 177 shows a nucleotide sequence (SEQ ID NO:314) of a native sequence PRO1431 (UNQ737) cDNA, wherein SEQ ID NO:314 is a close designated herein as *DNA73401-1633*. The start and stop codons are shown in bold and underlined font.

35 Figure 178 shows the amino acid sequence (SEQ ID NO:315) derived from the coding sequence of SEQ ID NO:314 shown in Figure 177.

Figures 179A-B show a nucleotide sequence (SEQ ID NO:316) of a native sequence PRO1563 (UNQ769) cDNA, wherein SEQ ID NO:316 is a close designated herein as "DNA73492-1671". The start and stop codons are shown in bold and underlined font.

Figure 180 shows the amino soid requence (SEQ ID NO.317) derived from the coding sequence of SEQ D NO.316 shown in Figures 179A-B.

Figure 181 shows a mucleotide sequence (SEQ ID NO:321) of a native sequence PRO1565 (UNQ771) cDNA, wherein SEQ ID NO:321 is a clone designated herein as "DNA73727-1673". The start and stop codons are shown in bold and undertined fom:

Figure 182 shows the amino acid sequence (SEQ ID NO:322) derived from the coding sequence of SEQ ID NO:321 shown in Figure 181.

Figure 183 shows a nucleotide sequence (SEQ ID NO:323) of a native sequence PRO1571 (UNQ777) cDNA, wherein SEQ ID NO:323 is a clone designated herein as "DNA73730-1679". The start and stop codons are shown in bold and underlined fort.

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Figure 184 shows the amino acid sequence (SEQ ID NO:324) derived from the coding sequence of SEQ ID NO:323 shown in Figure 183.

Figure 183 shows a nucleotide sequence (SEQ ID NO:325) of a native sequence PRO1572 (UNQ778) cDNA, wherein SEQ ID NO:325 is a clone designated herein as "DNA73734-1680". The start and stop codons are shown in bold and underlined four.

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Figure 186 shows the amino acid sequence (SEQ ID NO:326) derived from the coding sequence of SEQ ID NO:325 shown in Figure 185.

Figure 187 shows a nucleotide sequence (SEQ ID NO:327) of a native sequence PRO1573 (UNQ779) cDNA, wherein SEQ ID NO:327 is a clone designated herein as "DNA73735-1681". The start and stop codons are shown in bold and underlined font.

Figure 188 shows the amino acid sequence (SEQ ID NO:328) derived from the coding sequence of SEQ ID NO:327 shown in Figure 187.

Figure 189 shows a nucleotide sequence (SEQ ID NO:329) of a native sequence PRO1488 (JNQ757) cDNA, wherein SEQ ID NO:329 is a clone designated herein as "DNA73736-1657". The start and stop codons are shown in bold and underlined front.

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Figure 190 shows the amino acid sequence (SEQ ID NO:330) derived from the coding sequence of SEQ ID NO:329 shown in Figure 189.

Figure 191 shows a nucleotide sequence (SEQ ID NO:331) of a native sequence FRO1489 (UNQ758) cDNA, wherein SEQ ID NO:331 is a clone designated herein as "DNA73737-1658". The start and stop codons are shown in bold and underlined foru.

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Figure 192 shows the amino acid sequence (SEQ ID NO:332) derived from the coding sequence of SEQ ID NO:331 shown in Figure 191.

Figure 193 shows a nucleotide sequence (SEQ ID NO:333) of a native sequence PRO1474 (UNQ745) cDNA, wherein SEQ ID NO:333 is a clone designated herein as "DNA73739-1645". The start and stop codons are shown in bold and underlined fout.

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Figure 194 shows the amino acid sequence (SEQ ID NO:334) derived from the coding sequence of SEQ ID NO:333 shown in Figure 193.

Figure 195 shows a nucleotide sequence (SEQ ID NO:335) of a native sequence PRO1508 (UNQ761) cDNA, wherein SEQ ID NO:335 is a clone designated herein as "DNA73742-1662". The start and stop codons are shown in bold and underlined font.

Figure 196 shows the amino acid sequence (SEQ ID NO:336) derived from the coding sequence of SEQ ID NO:335 shown in Figure 195.

Figure 197 shows a nucleotide sequence (SEQ ID NO.337) of a native sequence PRO1555 (UNQ763) cDNA, wherein SEQ ID NO.337 is a clone designated herein as "DNA73744-1665". The start and stop codons are shown in bold and underlined font.

Figure 198 shows the amino acid sequence (SEQ ID NO:338) derived from the coding sequence of SEQ ID NO:337 shown in Figure 197.

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Figure 199 shows a nucleotide sequence (SEQ ID NO.339) of a native sequence PRO1485 (UNQ754) cDNA, wherein SEQ ID NO.339 is a clone designated herein as "DNA73746-1654". The start and stop codons are shown in bold and underlined font.

15 Figure 200 shows the amino acid sequence (SEQ ID NO.340) derived from the coding sequence of SEQ ID NO.339 shown in Figure 199.

Figure 201 shows a nucleotide sequence (SEQ ID NO:346) of a native sequence PRO1564 (UNQ770) cDNA, wherein SEQ ID NO:346 is a clone designated herein as *DNA73780-1672*. The start and stop codons are shown in bold and underlined font.

20 Figure 202 shows the amino sold sequence (SEQ ID NO:347) derived from the coding sequence of SEQ ID NO:346 shown in Figure 201.

Figure 203 shows a nucleoride sequence (SEQ ID NO:351) of a native sequence PRO1755 (UNQ828) cDNA, wherein SEQ ID NO:351 is a clone designated herein as "DNA76396-1698". The start and stop codons are shown in bold and underlined font.

25 Figure 204 shows the amino soid sequence (SEQ ID NO.352) derived from the coding sequence of SEQ ID NO.351 shown in Figure 203.

Figure 205 shows a nucleotide sequence (SEQ ID NO:353) of a native sequence PRO1757 (UNQ850) cDNA, wherein SEQ ID NO:353 is a clone designated herein as "DNA/6398-1699". The start and stop codons are shown in bold and underlined form.

30 Figure 206 shows the amino acid sequence (SEQ ID NO:354) derived from the coding sequence of SEQ ID NO:353 shown in Figure 205.

Figure 207 shows a nucleotide sequence (SEQ ID NO:355) of a native sequence PRO1758 (UNQ831) cDNA, wherein SEQ ID NO:355 is a close designated herein as "DNA76399-1700". The start and stop codons are shown in bold and underlined font.

35 Figure 208 shows the amino acid sequence (SEQID NO:356) derived from the coding sequence of SEQID NO:355 shown in Figure 207.

Figure 209 shows a nucleotide sequence (SEQ ID NO:357) of a native sequence PRO1575 (UNQ781) cDNA, wherein SEQ ID NO:357 is a clone designated herein as "DNA76401-1683". The start and stop codons are shown in bold and underlined font.

Figure 210 shows the amino acid sequence (SEQ ID NO:358) derived from the coding sequence of SEQ ID NO:357 shown in Figure 209.

Figure 211 shows a nucleonide sequence (SEQ ID NO:363) of a native sequence PRO1787 (UNQ849) cDNA, wherein SEQ ID NO:363 is a clone designated herein as "DNA76510-2504". The start and stop codons are shown in bold and maderlined form.

Figure 212 shows the amino acid sequence (SEQ ID NO:364) derived from the coding sequence of SEQ ID NO:363 shown in Figure 211.

Figure 213 shows a nucleotide sequence (SEQ ID NO.365) of a native sequence PRO1781 (UNQ843) cDNA, wherein SEQ ID NO.365 is a clone designated herein as "DNA76522-2500". The start and stop codons are shown in bold and underlined font.

Figure 214 shows the amino acid sequence (SEQ ID NO:366) derived from the coding sequence of SEQ ID NO:365 shown in Figure 213.

Figure 215 shows a nucleotide sequence (SEQ ID NO:371) of a native sequence PRO1556 (UNQ764) cDNA, wherein SEQ ID NO:371 is a clone designated herein as "DNA76529-1666". The start and stop codons are shown in boild and underlined from.

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Figure 216 shows the amino acid sequence (SEQ ID NO:372) derived from the coding sequence of SEQ ID NO:371 shown in Figure 215.

20 Figure 217 shows a nucleotide sequence (SEQ ID NO:373) of a native sequence PRO1759 (UNQ832) cDNA, wherein SEQ ID NO:373 is a clone designated herein as "DNA76531-1701". The start and stop codons are shown in bold and underlined font.

Figure 218 shows the amino acid sequence (SEQ ID NO:374) derived from the coding sequence of SEQ ID NO:373 shown in Figure 217.

Figure 219 shows a nucleotide sequence (SEQ ID NO:375) of a native sequence PRO1760 (UNQ833) cDNA, wherein SEQ ID NO:375 is a clone designated herein as "DNA76532-1702". The start and stop codous are shown in hold and underlined font.

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Figure 220 shows the amino acid sequence (SEQ ID NO.376) derived from the coding sequence of SEQ ID NO.375 shown in Figure 219.

Figure 221 shows a nucleotide sequence (SEQ ID NO:377) of a native sequence PRO1561 (UNQ768) cDNA, wherein SEQ ID NO:377 is a clone designated herein as "DNA76538-1670". The start and stop codons are shown in hold and underlined font.

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Figure 222 shows the amino acid sequence (SEQ ID NO:378) derived from the coding sequence of SEQ ID NO:377 shown in Figure 221.

35 Figure 223 shows a mucleotide sequence (SEQ ID NO:382) of a native sequence PRO1567 (UNQ773) cDNA, wherein SEQ ID NO:382 is a clone designated herein as "DNA76541-1675". The start and stop codons are shown in bold and underlined form.

oderlined form.

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Figure 224 shows the amino acid sequence (SEQ ID NO:383) derived from the coding sequence of SEQ ID NO:382 shown in Figure 223.

Figure 225 shows a nucleotide sequence (SEQ ID NO:384) of a native sequence PRO1693 (UNQ803) cDNA, wherein SEQ ID NO:384 is a clone designated herein as "DNA77301-1693". The start and stop codons are shown in bold and underlined form.

Figure 226 shows the amino acid sequence (SEQ ID NO:385) derived from the coding sequence of SEQ ID NO:384 shown in Figure 225.

Figure 227 shows a nucleoside sequence (SEQ ID NO:389) of a native sequence PRO1784 (UNQ846) cDNA, wherein SEQ ID NO:389 is a clone designated herein as "DNA77303:2502". The start and stop codous are shown in bold and underlined form.

Figure 228 shows the amino acid sequence (SEQ ID NO:390) derived from the coding sequence of SEQ ID NO:389 shown in Figure 227.

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Figure 229 shows a nucleotide sequence (SEQ ID NO:394) of a native sequence PRO1605 (JNQ786) cDNA, wherein SEQ ID NO:394 is a clone designated herein as *DNA77648-1688*. The start and stop codons are shown in bold and underlined font.

Figure 230 abows the amino acid sequence (SEQ ID NO:395) derived from the coding sequence of SEQ ID NO:394 shown in Figure 229.

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Figure 231 shows a nucleotide sequence (SEQ ID NO:396) of a native sequence PRO1788 (UNQ850) cDNA, wherein SEQ ID NO:396 is a close designated herein as "DNA77652-2505". The start and stop codons are shown in bold and underlined font.

20 Figure 232 shows the amino acid sequence (SEQ ID NO:397) derived from the coding sequence of SEC ID NO:396 shown in Figure 231.

Figure 233 shows a nucleotide sequence (SEQ ID NO:401) of a native sequence PRO1801 (UNQ852) cDNA, wherein SEQ ID NO:401 is a clone designated herein as "DNA83500-2506". The start and stop codons are shown in bold and underlined font.

25 Figure 234 shows the amino acid sequence (SEQ ID NO:402) derived from the coding sequence of SEQ ID NO:401 shown in Figure 233.

Figure 235 shows a nucleotide sequence (SEQ ID NO:405) of a native sequence UCP4 cDNA, wherein SEQ ID NO:405 is a clone designated herein as "DNA77568-1626". The start and stop codons are shown in bold and underlined font.

30 Figure 236 shows the amino acid sequence (SEQ ID NO:406) derived from the coding sequence of SEQ ID NO:405 shown in Figure 235.

Figure 237 shows a nucleotide sequence (SEQ ID NO:409) of a native sequence PRO193 cDNA, wherein SEQ ID NO:409 is a clone designated herein as "DNA23322-1393". The start and stop codons are shown in bold and underlined form.

35 Figure 238 shows the amino acid sequence (SEQ ID NO:410) derived from the coding sequence of SEQ ID NO:409 shown in Figure 237.

Figure 239 shows a nucleotide sequence (SEQ ID NO:414) of a native sequence PRO1130 cDNA, wherein SEQ ID NO:414 is a clone designated herein as "DNA59814-1486". The start and stop codons are shown in bold and underlined font.

Figure 240 shows the amino acid sequence (SEQ ID NO:415) derived from the coding sequence of SEQ D NO:414 shown in Figure 239.

Figure 241 shows a nucleotide sequence (SEQ ID NO:422) of a native sequence PRO1335 cDNA, wherein SEQ ID NO:422 is a clone designated herein as "DNA62812-1594". The start and stop codous are shown in bold and underlined funt.

Figure 242 shows the amino acid sequence (SEQ ID NO:423) derived from the coding sequence of SEQ ID NO:422 shown in Figure 241.

Figure 243 shows a nucleotide sequence (SEQ ID NO:428) of a native sequence PRO1329 cDNA, wherein SEQ ID NO:428 is a clone designated herein as "DNA66660-1585". The start and stop codons are shown in bold and underlined four.

Figure 244 shows the amino acid sequence (SEQ ID NO:429) derived from the coding sequence of SEQ ID NO:428 shown in Figure 243.

Figure 245 shows a nucleotide sequence (SEQ ID NO.430) of a native sequence PRO1550 cDNA. wherein SEQ ID NO.430 is a clone designated herein as "DNA76393-1664". The start and stop codons are shown in bold and underlined fort.

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Figure 246 shows the amino axid sequence (SEQ ID NO:431) derived from the coding sequence of SEQ ID NO:430 shown in Figure 245.

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Figures 247A-D show hypothetical exemplifications for using the below described method to determine % amino acid sequence identity (Figures 247A-B) and % nucleic acid sequence identity (Figures 247C-D) using the ALIGN-2 equence comparison computer program, wherein "PRO" represents the amino acid sequence of a bypothetical PEACH polypeptide of interest, "Comparison Protein" represents the amino acid sequence of a polypeptide sgainst which the "PRO" polypeptide of interest is being compared, "PRO-DNA" represents a bypothetical PEACH-encoding nucleic acid sequence of interest, "Comparison DNA" represents the nucleotide sequence of a nucleic acid molecule against which the "PRO-DNA" nucleic acid molecule of interest is being compared, "X, "Y" and "Z" each represent different hypothetical amino acid residues and "N", "L" and "V" each represent different hypothetical nucleotides.

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Figures 248A-Q provide the complete source code for the ALIGN-2 sequence comparison computer 30 program. This source code may be routinely compiled for use on a UNIX operating system to provide the ALIGN-2 sequence comparison computer program.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Delinitions

35 The terms "PRO polypeptide" and "PRO" or "UCP" as used herein and when immediately followed by a numerical designation refer to various polypeptides, wherein the complete designation (i.e., PRO/number) refers to specific polypeptide sequences as described herein. The terms "PRO/number polypeptide" and

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"PRO/aumber" wherein the term 'number' is provided as an actual numerical designation as used herein encompass native sequence polypeptides and polypeptide variants (which are further defined herein). The PRO polypeptides described herein may be isolated from a variety of sources, such as from human tissue types or from another source, or prepared by recombinant or synthetic methods.

A "native sequence PRO polypeptide" or "UCP" comprises a polypeptide having the same amino acid

5 sequence as the corresponding PRO polypeptide derived from nature. Such native sequence PRO polypeptides
can be isolated from nature or can be produced by recombinant or synthetic means. The term "native sequence
PRO polypeptide" specifically ensumpasses naturally-occurring transated or secreted forms of the specific PRO
polypeptide (e.g., an extracellular domain sequence), naturally-occurring variant forms (e.g., alternative)
spliced forms) and naturally-occurring allelic variants of the polypeptide. In various embodiments of the
invention, native sequence PRO polypeptides are mature or full-length native sequence polypeptides comprising
the full-length amino acids sequences shown in the accompanying figures. Start and stop codons are shown in
bold fornt and underlined in the figures. However, while the PRO polypeptide disclosed in the accompanying
figures are shown to begin with methionize residues designated herein as amino acid position 1 in the figures,
it is conceivable and possible that other methionine residues located either upstream or downstream from the
15 amino acid position 1 in the figures may be employed as the starting amino acid residue for the PRO
polypeptides.

The PRO polypeptide "extracellular domain" or "ECD" refers to a form of the PRO polypeptide which is essentially free of the transmembrane and cytoplasmic domains. Ordinarily, a PRO polypeptide ECD will have less than 1% of such transmembrane and cytoplasmic domains and preferably, will have less than 0.5% of such domains. It will be understood that any transmembrane domains identified for the PRO polypeptides of the present invention are identified pursuant to criteria routinely employed in the art for identifying that type of hydrophobic domain. The exact boundaries of a transmembrane domain may vary but most likely by no more than about 5 amino acids at either end of the domain as initially identified herein. Optionally, therefore, an extracellular domain of a PRO polypeptide may contain from about 5 or fewer amino acids on either side of the transmembrane domain/extracellular domain boundary as identified in the Examples or specification and such polypeptides, with or without the associated signal peptide, and nucleic acid encoding them, are contemplated by the present invention.

The approximate location of the "signal peptides" of the various PRO polypeptides disclosed herein are shown in the accompanying figures. It is noted, however, that the C-terminal boundary of a signal peptide C-terminal boundary of a signal peptide C-terminal boundary as initially identified herein, wherein the C-terminal boundary of the signal peptide may be identified boundary as initially identified herein, wherein the C-terminal boundary of the signal peptide may be identified pursuant to criteria routinely employed in the art for identifying that type of amino acid sequence element (e.g., Nielsen et al., Prot. Eng. 10:1-6 (1997) and von Heinje et al., Niel. Acids. Res. 14:4683-4690 (1986)). Moreover, it is also recognized that, in some cases, cleavage of a signal sequence from a secreted polypeptide is not entirely uniform, resulting in more than one secreted species. These mature polypeptides, where the signal peptide is cleaved within no more than about 5 amino acids on either side of the C-terminal boundary of the signal peptide as identified herein, and the polypsucleotides encoting them, are contemplated by the present

invention

25 8 15 ö a full-length PRO polypeptide sequence as disclosed herein. Such PRO polypeptide variants include, for length, more often at least about 50 amino acids in length, more often at least about 60 amino acids in length, sequence identity, more preferably at least about 84 % amino acid sequence identity, more preferably at least at least about 90 amino acids in length, more often at least about 100 amino acids in length, more often at least more often at least about 70 amino acids in length, more often at least about 80 amino acids in length, more often preferably at least about 92% amino acid sequence identity, more preferably at least about 93% amino acid 300 amino acids in length, or more. as disclosed herein, an extracellular domain of a PRO polypoptide, with or without the signal peptide, as sequence PRO polypeptide sequence as disclosed herein, a PRO polypeptide sequence lacking the signal peptide preferably at least about 87% amino acid sequence identity, more preferably at least about 88% amino acid about 150 amino acids in length, more often at least about 200 amino acids in length, more often at least about acids in length, more often at least about 30 amino acids in length, more often at least about 40 amino acids in Ordinarily, PRO variant polypeptides are at least about 10 amino acids in length, often at least about 20 amino disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein preferably at least about 97% amino acid sequence idemity, more preferably at least about 98% amino acid about 95 % amino acid sequence identity, more preferably at least about 96 % amino acid sequence identity, more sequence identity, more preferably at least about 94 % amino acid sequence identity, more preferably at least sequence identity, more preferably at least about 89% amino acid sequence identity, more preferably at least about 85 % amino acid sequence identity, more preferably at least about 86 % amino acid sequence identity, more preferably at least about 82% amino acid sequence identity, more preferably at least about 83% amino acid about 80% amino acid sequence identity, preferably at least about 81% amino acid sequence identity, more terminus of the full-length native amino acid sequence. Ordinarily, a PRO polypeptide variant will have at least instance, PRO polypeptides wherein one or more amino acid residues are added, or deleted, at the N- or Cdomain of a PRO polypeptide, with or without the signal peptide, as disclosed herein or any other fragment of equence identity and most preferably at least about 99% amino acid sequence identity with a full-length native about 90% amino acid sequence identity, more preferably at least about 91% amino acid sequence identity, more disclosed herein, a PRO polypeptide sequence lacking the signal peptide as disclosed herein, an extracellular about 80% amino acid sequence identity with a full-length native sequence PRO polypoptide sequence as *PRO polypeptide variant" means an active PRO polypeptide as defined above or below having at leas

"Percent (%) amino acid sequence identity" with respect to the PRO polypeptide sequences identified berein is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific PRO polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed

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to achieve maximal alignment over the full length of the sequences being compared. For purposes herein, however, % amino acid sequence identity values are generated using the WU-BLAST-2 computer program (Altschul et al., Methods in Emzymology 266:460-480 (1996)): Most of the WU-BLAST-2 search parameters are set to the default values. Those not set to default values, i.e., the adjustable parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix 5 = BLOSUM62. For purposes herein, a % amino acid sequence identity value is determined by dividing (a) the number of matching identical amino acid residues between the amino acid sequence of the PRO polypeptide of interest having a sequence against which the PRO polypeptide of interest is being compared which may be a PRO variant polypeptide) as determined by WU-BLAST-2 by (b) the total number of amino acid residues of the PRO polypeptide of interest having an the amino acid sequence A which has or having at least 80% amino acid sequence identity to the amino acid sequence B*, the amino acid sequence A is the comparison amino acid sequence of interest and the amino acid sequence B is the amino acid sequence of the PRO polypeptide of the PRO polypeptid

Unless specifically stated otherwise, all % amino acid sequence identity values used herein are obtained

15 as described in the immediately preceding paragraph using the WU-BLAST-2 computer program. However,

% amino acid sequence identity values may also be obtained as described below by using the sequence
comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is
provided in Figures 248A-Q. The ALIGN-2 sequence comparison computer program was authored by
Generatech, Inc. and the source code shown in Figures 248A-Q has been filed with user documentation in the

20 U.S. Copyright Office, Weshington D.C., 20559, where it is registered under U.S. Copyright Registration No.
TXU510087. The ALIGN-2 program is publicly available through Genemech, Inc., South San Francisco,
California or may be compiled from the source code provided in Figures 248A-Q. The ALIGN-2 program
ahould be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence
comparison parameters are set by the ALIGN-2 program and do not vary.

25 In situations where ALIGN-2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

100 times the fraction X/Y

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where X is the number of amino acid residues scored as identical matches by the sequence alignment program

ALIGN-2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in

B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid

sequence B, the % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of

B to A. As examples of % amino acid sequence identity calculations using this method, Figures 247A-B

demonstrate how to calculate the % amino acid sequence identity of the amino acid sequence designated

"Comparison Protein" to the amino acid sequence designated "PRO"

Percent amino acid sequence identity may also be determined using the sequence comparison program NCB1-BLAST? (Altachul et al., Nieleic Acids Res., 25:3389-3402 (1997)). The NCB1-BLAST? sequence comparison program may be downloaded from http://www.ncbi.nlm.nih.gov. NCB1-BLAST? uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

In situations where NCBI-BLAST2 is employed for amino acid sequence comparisons, the % amino acid sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (0) (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % amino acid sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

100 times the fraction X/Y

- 15 where X is the number of amino acid residues scored as identical triatches by the sequence alignment program NCBI-BLAST2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, this % amino acid sequence identity of A to B will not equal the % amino acid sequence identity of B to A.
- 딿 30 25 20 preferably at least about 94% nucleic acid sequence identity, more preferably at least about 95% nucleic acid disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. sequence identity, more preferably at least about 96% nucleic acid sequence identity, more preferably at least nucleic acid sequence identity, more preferably at least about 93% nucleic acid sequence identity, more least about 89% nucleic acid sequence identity, more preferably at least about 90% nucleic acid sequence acid sequence identity, more preferably at least about 88% nucleic acid sequence identity, more preferably at more preferably at least about 86% nucleic acid sequence idently, more preferably at least about 87% nucleic about 84% nucleic acid sequence identity, more preferably at least about 85% nucleic acid sequence identity, preferably at least about 81% nucleic acid sequence identity, more preferably at least about 82% nucleic acid Ordinarily, a PRO variant polynucleotide will have at least about 80% nucleic acid sequence identity, more sequence identity with a nucleotide acid sequence encoding a full-length native sequence PRO polypeptide which encodes an active PRO polypeptide as defined below and which has at least about 80% nucleic acid idenity, more preferably at least about 91% nucleic acid sequence identity, more preferably at least about 92% as disclosed herein, an extracellular domain of a PRO polypeptide, with or without the signal peptide, as sequence identity, more preferably at least about 83 % nucleic acid sequence identity, more preferably at least requence as disclosed herein, a full-length native sequence PRO polypeptide sequence lacking the signal peptide "PRO variant polynucleotide" or "PRO variant nucleic acid sequence" means a nucleic acid molecule

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yet more preferably at least about 99% nucleic acid sequence identity with the nucleic acid sequence encoding a full-length native sequence PRO polypeptide sequence as disclosed herein, a full-length native sequence PRO polypeptide sequence to disclosed herein, an extracellular domain of a PRO polypeptide sequence lacking the signal peptide as disclosed herein or any other fragment of a full-length PRO polypeptide, with or without the signal sequence, as disclosed herein or any other fragment of a full-length PRO polypeptide sequence as disclosed herein. Variants do not encompass the native nucleotide sequence.

Ordinatily, PRO variant polynucleotides are at least about 20 nucleotides in length, often at least about 60 nucleotides in length, more often at least about 90 nucleotides in length, more often at least about 120 nucleotides in length, more often at least about 120 nucleotides in length, more often at least about 180 nucleotides in length, more often at least about 180 nucleotides in length, more often at least about 240 nucleotides in length, more often at least about 240 nucleotides in length, more often at least about 300 nucleotides in length, more often at least about 450 nucleotides in length, more often at least about 600 nucleotides in length, more often at least about 600 nucleotides in length, more often at least about 600 nucleotides in length, or more.

æ 25 20 5 sequence identity to the nucleic acid sequence B*, the nucleic acid sequence A is the comparison nucleic acid molecule of interest and the nucleic acid sequence B is the nucleic acid sequence of the PRO polypeptide nucleic acid molecule comprising a nucleic acid sequence A which has or having at least 80% nucleic acid of the PRO polypeptide-encoding nucleic acid molecule of interest. For example, in the statement "an isolated may be a variant PRO polynucleoside) as determined by WU-BLAST-2 by (b) the total number of nucleosides sequence against which the PRO polypeptide-encoding nucleic acid molecule of interest is being compared which sequence PRO polypeptide-encoding nucleic acid and the comparison nucleic acid molecule of interest (i.e., the the PRO polypeptide-encoding nucleic acid molecule of interest having a sequence derived from the native parameters, are set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) BLAST-2 scarch parameters are set to the default values. Those not set to default values, i.e., the adjustable necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent encoding nucleic acid molecule of interest. determined by dividing (a) the number of matching identical nucleotides between the nucleic acid sequence of = 11, and scoring matrix = BLOSUM62. For purposes herein, a % nucleic acid sequence identity value is BLAST-2 computer program (Alaschul et al., Methods in Enzymology, 266:460-480 (1996)). Most of the WUusing publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. For purposes herein, however, % nucleic acid sequence identity values are generated using the WUnucleic acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, nucleotides in the PRO nucleic acid sequence of interest, after aligning the sequences and introducing gaps, if identified herein is defined as the percentage of nucleotides in a candidate sequence that are identical with the *Percent (\$) nucleic acid sequence identity" with respect to PRO-encoding nucleic acid sequences

Unless specifically stated otherwise, all % nucleic acid sequence identity values used berein are obtained as described in the immediately preceding paragraph using the WU-BLAST-2 computer program. However, 35 % nucleic acid sequence identity values may also be obtained as described helow by using the sequence comparison computer program ALIGN-2, wherein the complete source code for the ALIGN-2 program is provided in Figures 248A-Q. The ALIGN-2 sequence comparison computer program was ambored by

about 97% nucleic acid sequence identity, more preferably at least about 98% nucleic acid sequence identity and

Generatech, Inc. and the source code shown in Figures 248A-Q has been filed with user documentation in the U.S. Copyright Office. Washington D.C., 20559, where it is registered under U.S. Copyright Registration No. TXUS10087. The ALIGN-2 program is publicly available through Generatech, Inc., South San Francisco, California or may be compiled from the source code provided in Figures 248A-Q. The ALIGN-2 program should be compiled for use on a UNIX operating system, preferably digital UNIX V4.0D. All sequence comparison parameters are set by the ALIGN-2 program and do not vary.

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In situations where ALIGN-2 is employed for nucleic acid sequence comparisons, the % nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

100 times the fraction W/Z

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where W is the number of nucleoides scored as identical matches by the sequence alignment program ALIGN-2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to C. As examples of % nucleic acid sequence identity calculations, Figures 247C-D demonstrate how to calculate the % nucleic acid sequence identity of the nucleic acid sequence designated "Comparison DNA" to the nucleic acid sequence designated "PRO-DNA".

Percent nucleic acid requence identity may also be determined using the sequence comparison program NCBI-BLAST2 (Altschul et al., Nucleic Acids Res., 25:3389-3402 (1997)). The NCBI-BLAST2 requence comparison program may be downloaded from http://www.ncbi.nlm.nih.gov. NCBI-BLAST2 uses several search parameters, wherein all of those search parameters are set to default values including, for example, unmask = yes, strand = all, expected occurrences = 10, minimum low complexity length = 15/5, multi-pass e-value = 0.01, constant for multi-pass = 25, dropoff for final gapped alignment = 25 and scoring matrix = BLOSUM62.

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In sinutions where NCBi-BLAST2 is employed for sequence comparisons, the & nucleic acid sequence identity of a given nucleic acid sequence C to, with, or against a given nucleic acid sequence D (which can alternatively be phrased as a given nucleic acid sequence C that has or comprises a certain % nucleic acid

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100 times the fraction W/Z

sequence identity to, with, or against a given nucleic acid sequence D) is calculated as follows:

where W is the number of nucleotides scored as identical matches by the sequence alignment program NCBI35 BLAST2 in that program's alignment of C and D, and where Z is the total number of nucleotides in D. It will
be appreciated that where the length of nucleic acid sequence C is not equal to the length of nucleic acid sequence
D, the % nucleic acid sequence identity of C to D will not equal the % nucleic acid sequence identity of D to

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In other embodiments, PRO variant polynucleotides are nucleic acid molecules that encode an active PRO polypeptide and which are capable of hybridizing, preferably under stringent hybridization and wash conditions, to nucleotide sequences encoding a full-length PRO polypeptide as disclosed herein. PRO variant polypeptides may be those that are encoded by a PRO variant polynucleotide.

The term "positives", in the context of sequence comparison performed as described above, includes residues in the sequences compared that are not identical but have similar properties (e.g., as a result of conservative substitutions, see Table 1 below). For purposes herein, the % value of positives is determined by dividing (a) the number of amino acid residues secoring a positive value between the PRO polypeptide amino acid sequence of interest having a sequence derived from the native PRO polypeptide sequence and the comparison and sequence of interest (i.e., the amino acid sequence against which the PRO polypeptide sequence is being compared) as determined in the BLOSUM62 matrix of WU-BLAST-2 by (b) the total number of amino acid residues of the PRO polypeptide of interest.

Unless specifically stated otherwise, the % value of positives is calculated as described in the immediately preceding paragraph. However, in the context of the amino acid sequence identity comparisons 15 performed as described for ALIGN-2 and NCBI-BLAST2 above, includes amino acid residues in the sequences compared that are not only identical, but also those that have similar properties. Amino acid residues that score a positive value to mainton acid residue of interest are those that are either identical to the amino acid residue of interest or are a preferred substitution (as defined in Table 1 below) of the amino acid residue of interest.

For amino acid sequence comparisons using ALIGN-2 or NCBI-BLAST2, the % value of positives of 20 a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % positives to, with, or against a given amino acid sequence B) is calculated as follows:

100 times the fraction X/Y

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where X is the number of amino acid residues scoring a positive value as defined above by the sequence alignment program ALIGN-2 or NCBI-BLAST2 in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % positives of A to B will not equal the % positives of B to A.

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"Isolated," when used to describe the various polypeptides disclosed herein, means polypeptide that has been identified and separated and/or recovered from a component of its natural environment. Comaminant components of its natural environment are materials that would typically interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous so solutes. In preferred embodiments, the polypeptide will be purified (1) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (2) to homogeneity by SDS-PAGE under non-reducing or reducing conditions using Coomassie blue or, preferably.

silver sain. Isolated polypeptide includes polypeptide in situ within recombinant cells, since at least one component of the PRO polypeptide natural environment will not be present. Ordinarily, however, isolated polypeptide will be prepared by at least one purification step.

An "isolated' PRO polypeptide-encoding nucleic acid is a nucleic acid molecule that is identified and separated from at least one contaminant nucleic acid molecule with which it is ordinarily associated in the natural source of the PRO polypeptide nucleic acid. An isolated PRO polypeptide nucleic acid molecule is other than in the form or setting in which it is found in nature. Isolated PRO polypeptide nucleic acid molecules therefore are distinguished from the specific PRO polypeptide nucleic acid molecule as it exists in natural cells. However, an isolated PRO polypeptide nucleic acid molecule in cells that ordinarily express the PRO polypeptide where, for example, the nucleic acid molecule is in a chromosomal location different from that of natural cells.

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The term 'control sequences' refers to DNA sequences necessary for the expression of an operably instead coding sequence in a particular host organism. The control sequences that are suitable for prokaryones, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

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Nucleic acid is 'operably linked' when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polyperpide if it is expressed as a prepriorien that participates in the secretion of the polyperpide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, 20 "operably linked means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oilgonucleoxide adaptors or linkers are used in accordance with conventional practice.

The term 'antibody' is used in the broadest sense and specifically covers, for example, single anti-PRO monoclonal antibodies (including agonist, antagonist, and neutralizing antibodies), anti-PRO antibody compositions with polyepitopic specificity, single chain anti-PRO antibodies, and fragments of anti-PRO antibodies (see below). The term 'monoclonal antibody' as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally-occurring mutations that may be present in minor amounts.

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Stringency* of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe length, washing temperature, and sail concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower temperatures. Hybridization generally depends on the ability of denatured DNA to reanneal when complementary strands are present in an environment below their melting temperature. The higher the degree of desired homology between the probe and hybridizable sequence, the higher the relative temperature which can be used. As a result, it follows that higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of

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hybridization reactions, see Ausubel et al., <u>Ourrent Protocols in Molecular Biology</u>, Wiley Interscience Publishers, (1995).

"Stringent conditions" or 'high stringency conditions", as defined herein, may be identified by those that: (1) employ low ionic strength and high temperature for washing, for example 0.015 M sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C; (2) employ during hybridization a 5 demanuring agent, such as formanide, for example, 50% (v/v) formanide with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinyleyrrolidone/50mMsodium phosphate buffer ai pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42°C; or (3) employ 50% formanide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6.8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, somicated salmon sperm DNA (50 µg/ml), 0.1% SDS, and 10% destran sulfate at 42°C, with washes at 42°C of in 0.2 x SSC (sodium chloride/sodium citrate) and 50% formanide at 55°C, followed by a high-stringency wash

"Moderately stringent conditions" may be identified as described by Sambrook et al., Molecula Chming: A Laborstory Manual, New York: Cold Spring Harbor Press, 1989, and include the use of washing solution and hybridization conditions (e.g., temperature, ionic strength and %SDS) less stringent that those 15 described above. An example of moderately stringent conditions is overnight incubation at 37°C in a solution comprising: 20% formamide, 5 x SSC (150 mM NaCl. 15 mM trisodium citrate). 50 mM sodium phosphate (pH 7.6), 5 x Dembardt's solution, 10% destron sulfate, and 20 mg/ml denatured sheared salmon sperm DNA.

consisting of 0.1 x SSC containing EDTA at 55°C.

comprising: 20% formamide, 5 x SSC (150 mM NaCl, 15 mM utsodium citrate), 50 mM asotium phosphate (pH 7.6), 5 x Denhardt's solution, 10% dextran sulfate, and 20 mg/ml denatured sheared salmon sperm DNA, followed by washing the filters in 1 x SSC at about 37-30°C. The skilled artisan will recognize how to adjust the temperature, ionic streagth, etc. as necessary to accommodate factors such as probe length and the like.

The term "epitope tagged" when used herein refers to a chimeric polypeptide comprising a PRO

polypeptide fused to a 'tag polypeptide'. The tag polypeptide to comply residues to provide an epitope against which an antibody can be made, yet is short enough such that it does not interfere with activity of the polypeptide to which it is fused. The tag polypeptide preferably also is fairly unique to that the amibody does not substantially cross-react with other epitopes. Suitable tag polypeptides generally have at least six amino acid residues and usually between about 8 and 50 amino acid residues (preferably, between about 10 and 20 amino acid residues).

As used herein, the term "immunoadhesin" designates ambody-like molecules which combine the binding specificity of a heterologous protein (an "adhesin") with the effector functions of immunoglobulin constant domains. Structurally, the immunoadhesins comprise a fusion of an amino acid sequence with the 30 desired binding specificity which is other than the antigen recognition and binding site of an antibody (i.e., is "heterologous"), and an immunoglobulin constant domain sequence. The adhesin part of an immunoadhesin molecule typically is a contiguous amino acid sequence comprising at least the binding site of a receptor or a liguard. The immunoglobulin constant domain sequence in the immunoadhesin may be obtained from any immunoglobulin, such as 1gG-1, 1gG-2, 1gG-3, or 1gG-4 subtypes, 1gA (including 1gA-1 and 1gA-2), 1gE, 1gD 35 or 1gM.

"Active" or "activity" for the putposes herein refers to form(s) of a PRO polypeptide which retain a biological and/or an immunological activity of native or naturally-occurring PRO, wherein "biological" activity

or naturally-occurring PRO and an "immunological" activity refers to the ability to induce the production of an other than the ability to induce the production of an antibody against an antigenic epitope possessed by a native anihody against an antigenic epitope possessed by a native or naturally-occurring PRO. refers to a biological function (either inhibitory or stimulatory) caused by a native or naturally-occurring PRO

S identifying agonists or antagonists of a PRO polypeptide may comprise contacting a PRO polypeptide with a normally associated with the PRO polypeptide. candidate agonist or antagonist molecule and measuring a detectable change in one or more biological activities include agenist or antagonist antibodies or amibody fragments, fragments or amino acid sequence variants of maturer, the term "agonist" is used in the broadest sense and includes any molecule that mimics a biological blocks, inhibits, or neutralizes a biological activity of a native PRO polypeptide disclosed herein. In a similar native PRO polypeptides, peptides, antisense oligonucleotides, small organic molecules, etc. Methods for activity of a native PRO polypeptide disclosed herein. Suitable agonist or antagonist molecules specifically The term "aniagonist" is used in the broadest sense, and includes any molecule that partially or full

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treatment include those already with the disorder as well as those prone to have the disorder or those in whom the disorder is to be prevented. the object is to prevent or slow down (lessen) the targeted pathologic condition or disorder. Those in need of "Treatment" refers to both therapeutic treatment and prophylactic or preventative measures, wherein

"Intermittent" administration is treatment that is not consecutively done without interruption, but rather is cyclic an acute mode, so as to maintain the initial therapeutic effect (activity) for an extended period of time "Chronic" administration refers to administration of the agent(s) in a continuous mode as opposed to

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rabbits, etc. Preferably, the mammal is human. domestic and farm animals, and zoo, sports, or pet animals, such as dogs, cats, cattle, horses, sheep, pigs, gosts, "Mammal" for purposes of treatment refers to any animal classified as a mammal, including humans

(concurrent) and consecutive administration in any order. Administration "in combination with" one or more further therapeutic agents includes simultaneous

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ascorbic acid; low molecular weight (less than about 10 residues) polypeptide; proteins, such as serum albumin, the physiologically acceptable carrier is an aqueous pH buffered solution. Examples of physiologically gelatia, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidene; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including are nomexic to the cell or mammal being exposed thereto at the dosages and concentrations employed. Often forming counterious such as sodium; and/or nonionic surfactants such as TWEENT, polyethylene glycol (PEG) glucose, mannose, or dexirins; cholating agents such as EDTA; sugar alcohols such as mamitol or sorbitol; sale acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including "Carriers" as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers which

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variable region of the intox antibody. Examples of antibody fragments include Fab, Fab', F(ab') 2, and Fv "Annibody fragments" comprise a portion of an intact antibody, preferably the antigen binding or 35

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antibody molecules; and multispecific antibodies formed from antibody fragments. fragments; diabodies; linear antibodies (Zapata et al., Protein Eng. 8(10): 1057-1062 [1995]); single-chain

and is still capable of cross-linking antigen. ability to crystallize readily. Pepsin treatment yields an F(ab'), fragment that has two antigen-combining sites fragments, each with a single amigen-binding site, and a residual "Pc" fragment, a designation reflecting the Papain digestion of antibodies produces two identical antigen-binding fragments, called 'Fab'

to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific binding site on the surface of the VH-VL dimer. Collectively, the six CDRs confer antigen-binding specificity for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding association. It is in this configuration that the three CDRs of each variable domain interact to define an antigensite. This region comists of a dimer of one heavy- and one light-chain variable domain in tight, non-covalent "Fv" is the minimum antibody fragment which contains a complete antigen-recognition and -binding

a free thiol group. F(ab); antibody fragments originally were produced as pairs of Fab' fragments which have carboxy terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge hinge cysteines between them. Other chemical couplings of anibody fragments are also known. region. Fab'-SH is the designation herein for Fab' in which the cyrteine residue(3) of the constant domains bear (CH1) of the heavy chain. Fab fragments differ from Fab' fragments by the addition of a few residues at the The Fah fragment also contains the constant domain of the light chain and the first constant domain

20 of two clearly distinct types, called kappa and lambda, based on the amino acid sequences of their constant The "light chains" of antibodies (immunoglobulins) from any vertebrate species can be assigned to one

25 lgM, and several of these may be further divided into subclasses (isotypes), e.g., 1gG1, 1gG2, 1gG3, 1gG4, 1gA can be assigned to different classes. There are five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and Depending on the amino acid sequence of the constant domain of their heavy chains, immunoglobuling

30 antigen binding. For a review of sFv, see Pluckthun in The Pharmacology of Monoclonal Antibodies, vol. 113 polypeptide linker between the VH and VL domains which enables the sFv to form the desired structure for these domains are present in a single polypeptide chain. Preferably, the Fv polypeptide further comprises a "Single-chain Fv" or 'sFv" antibody fragments comprise the VH and VL domains of antibody, wherein

Rosenburg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994).

33 two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and on the same chain, the domains are forced to pair with the complementary domains of another chain and create same polypeptide chain (VH - VL). By using a linker that is too short to allow pairing between the two domains fragments comprise a heavy-chain variable domain (VH) connected to a light-chain variable domain (VL) in the The term "diabodies" refers to small antibody fragments with two antigen-binding sites, which

Hollinger et al., Proc. Natl. Acad. Sci. USA, 90:6444-6448 (1993). An "isolated" antibody is one which has been identified and separated and/or recovered from a

component of its natural environment. Contaminant components of its natural environment are materials which would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody will be purified (1) to greater than 95% by weight of antibody as determined by the Lowry method, and most preferably more than 99% by weight, (2) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or norarchacing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the amibody in situ within recombinant cells since at least one component of the amibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step.

The word 'label' when used herein refers to a detectable compound or composition which is conjugated

10 directly or indirectly to the antibody so as to generate a 'labeled' antibody. The label may be detectable by itself

(c.g. radioisouspe labels or fluorescent tabels) or, in the case of an enzymatic label, may catalyze chemical

alteration of a substrate compound or composition which is detectable.

By "solid phase" is meant a non-aqueous matrix to which the antibody of the present invention can adhere. Examples of solid phases encompassed herein include those formed partially or entirely of glass (e.g., 15 controlled pore glass), polysaccharides (e.g., agarose), polysacylamides, polysayrene, polyvinyl alcohol and silicones. In certain embodiments, depending on the context, the solid phase can comprise the well of an assay plate; in others it is a partification column (e.g., an affinity chromatography column). This term also includes a discontinuous solid phase of discrete particles, such as those described in U.S. Patent No. 4,275,149.

A "liposome" is a small vesicle composed of various types of lipids, phospholipids and/or surfactant

20 which is useful for delivery of a drug (such as a PRO polypeptide or antibody thereto) to a mammal. The
components of the liposome are commonly arranged in a bilayer formation, similar to the lipid arrangement of
biological membranes.

A "small molecule" is defined herein to have a molecular weight below about 500 Daltons.

25 II. Compositions and Methods of the Invention

The present invention provides newly identified and isolated nucleotide sequences encoding polypepides referred to in the present application as PRO polypepides. In particular, cDNAs encoding various PRO polypepides have been identified and isolated, as disclosed in further detail in the Examples below. It is noted has proteins produced in separate expression rounds may be given different PRO numbers but the UNQ number is unique for any given DNA and the encoded protein, and will not be changed. However, for sake of simplicity, in the present specification the protein encoded by the full length native nucleic acid molecules disclosed herein as well as all further native homologues and variants included in the foregoing definition of

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PRO, will be referred to as "PRO/aumber", regardless of their origin or mode of preparation.

As disclosed in the Examples below, various cDNA clones have been deposited with the ATCC. The
actual nucleotide sequences of those clones can readily be determined by the skilled artisan by sequencing of the

actual nucleotide sequences of those clones can readily be determined by the skilled artisan by sequencing of the deposited clone using routine methods in the art. The predicted armino acid sequence can be determined from the nucleotide sequence using routine skill. For the PBO polypeptides and encoding nucleic acids described

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herein. Applicants have identified what is believed to be the reading frame best identifiable with the sequence information available at the time.

Full-Length PRO Polypentides

1. PRO1560

Using the WU-BLAST2 sequence alignment computer program, the full-length native sequence PRO1560 (shown in Figure 2 and SEQ ID NO:4) has certain amino acid sequence identity with Tspan-6, identified after the discovery of the present invention berein. Accordingly, it is presently believed that PRO1560 disclosed in the present application is a newly identified member of the tetraspan family.

10 2. PRO44

The DNA26846-1397 clone was Isolated from a human feral lung library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA26846-1397 clone encodes a secreted factor. As far as is known, the DNA26846-1397 sequence encodes a novel factor designated herein as PRO444. Using the WU-BLAST2 sequence alignment computer program, no significant sequence identity with known proteins was revealed.

PRO1018

The DNA56107-1415 clone was isolated from a human ovary tumor tistue library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. As far as is known, the DNA56107-1415 sequence encodes a novel factor designated herein as PRO1018; using the WU-BLAST2 sequence alignment computer program, no significant sequence identities to any known proteins were revealed.

4. PRO1773

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the 25 full-length native sequence PRO1773 (shown in Figure 8 and SEQ ID NO: 10) has certain amino acid sequence identity with a portion of the retinol dehydrogenase type II protein of ratus norvegicus (ROH2_RAT). Accordingly, it is presently believed that PRO1773 disclosed in the present application is a newly identified member of the retinol dehydrogenase protein family and may possess activity typical of that protein family.

5. PRO1477

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Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1477 (shown in Figure 10 and SEQ ID NO:12) has certain amino acid sequence identity with the mannosyl-oligosaccharide 1.2-alpha-mannosidase protein (A54408). Accordingly, it is presently believed that PRO1477 disclosed in the present application is a newly identified member of the mannosidase protein family and may possess activity typical of the mannosidase protein family.

PROL

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1478 (abown in Figure 12 and SEQ ID NO:17) has certain amino acid sequence identity with galactoxyltransferases. Accordingly, it is presently believed that PRO1478 disclosed in the present application is a newly identified member of the galactoxyltransferase family and may possess at least one shared mechanism with other members of this family.

PRO831

The DNA56862-1343 clone was isolated from a human uterus library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA56862-1343 clone does encode a secreted factor. As far as is known, the DNA56862-1343 sequence encodes a novel factor designated herein as PRO831; using the WU-BLAST2 sequence alignment computer program, no sequence identifies to any known proteins were revealed.

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PROTIL

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-leagth native sequence PRO1113 (shown in Figure 16 and SEQ ID NO:24) has certain amino acid sequence identity with LIG-1 and SLIT. Accordingly, it is presently believed that PRO1113 disclosed in the present application is a newly identified member of the loucine rich repeat family and may possess protein-protein interaction activity as to typical of this family.

PRO1194

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As far as is known, the DNA57841-1522 sequence encodes a novel factor designated herein as PRO1194; using WU-BLAST2 sequence alignment computer programs, limited sequence identities to known proteins were revealed.

10. PROIL

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Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1110 (shown in Figure 20 and SEQ ID NO.31) has certain amino seld sequence identity with the murine myeloid upregulated protein. Accordingly, it is presently believed that PRO1110 disclosed in the present application is a newly identified member of the myeloid upregulated protein family and may possess activity typical of that family.

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11. PRO1378

The DNAS8730-1607 clone was isolated from a bone marrow library using a trapping technique which 35 selects for nucleotide sequences encoding secreted proteins. Thus, the DNAS8730-1607 clone encodes a secreted factor. As far as is known, the DNAS8730-1607 sequence encodes a novel factor designated herein as PRO1378. WU-BLAST2 sequence alignment computer programs revealed some sequence identities between

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the amino acid sequence of PRO1378 with known proteins. However, they were determined to not be significant.

12. PRO1481

As far as is known, the DNA58732-1650 sequence encodes a novel factor designated herein as PRO1481. Using WU-BLAST2 sequence alignment computer programs, only some sequence identities to known proteins were revealed.

3. PRO1189

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native

10 sequence PRO1189 (abown in Figure 26 and SEQ ID NO:43) has certain amino acid sequence identity with the
amino acid sequence of an E25 protein designated "MUSE25A_1" in the Dayhoff database. Accordingly, it is
presently believed that PRO1189 disclosed in the present application is a newly identified member of the E25
protein family and may possess activity or properties typical of that family.

15 14. PRO1415

The DNAS8852-1637 clone was isolated from a diseased human prostate tissue library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. As far as is known, the DNAS8852-1637 sequence encodes a novel factor designated herein as PRO1415; using the WU-BLAS77 sequence alignment computer program, no significant sequence identities to any known proteins were revealed.

I.S. PRO

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As far as is known, the DNA59212-1627 sequence encodes a novel factor designated herein as PRO1411. However, using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

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As far as is known, the DNA59218-1559 sequence encodes a novel factor designated herein as PRO1295. Using WU-BLAST72sequence alignment computer programs, only some sequence identities to known proteins were revealed.

17. PRO1359

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1359 (shown in Figure 34 and SEQ ID NO.56) has cortain amino acid sequence identity with N-acrylgaliotosamine alpha-2, 6-sialyltransferase. Accordingly, it is presently believed that PRO1359 disclosed in the present application is a newly identified member of the sialyltransferase family and may possess transferase

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activity typical of this family.

PROJISO

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1190 (shown in Figure 36 and SEQ ID NO.58) has certain amino acid requence identity with both rat and human CDO. Accordingly, it is presently believed that PRO1190 disclosed in the present application is a newly identified member of the CDO family and may possess cell adhesion activity typical of the CDO family.

· PRO1772

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1772 (abown in Figure 38 and SEQ ID NO:63) has certain amino acid sequence 10 identity with a human microsomal dipeptidase protein (P_R13857). Accordingly, it is presently believed that PRO1772 disclosed in the present application is a newly identified member of the peptidase protein family and may possess activity typical of that protein family.

0. PRO124

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length rative sequence PRO1248 (shown in Figure 40 and SEQ ID NO:68) has amino acid sequence identity with the PUT-2 protein (AF026188_5). Accordingly, it is presently believed that PRO1248 disclosed in the present application is a newly PUT-2 homolog and may possess activity typical of the PUT-2 protein.

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1316 (shown in Figure 42 and SEQ ID NO:70) has certain amino acid requence identity with murine dicktopf. Accordingly, it is presently believed that PRO1316 disclosed in the present application is a newly identified member of the dicktopf family and may possess the ability to cause head induction from the Spemann organizer and/or Writ aniagonism.

22. PRO119

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As far as is known, the DNA60611-1524 sequence encodes a novel factor designated berein as PRO1197. Using WU-BLAST2 sequence alignment computer programs, only some sequence identities to known proteins were revealed as further described in the examples.

23. PRO1293

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Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1293 (shown in Figure 46 and SEQ ID NO:77) has certain amino acid sequence identity 35 with the human Ig heavy chain V region protein (HSVCD54_1). Accordingly, it is presently believed that PRO1293 disclosed in the present application is a newly identified member of the Ig superfamily of proteins and fragments thereof and may possess activity typical of that family.

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4. PRO1380

The DNA60740-1615 clone was isolated from a human retina library. As far as is known, the DNA60740-1615 sequence encodes a novel multi-span transmembrane polypeptide designated herein as PRO1380. Using WU-BLAST2 sequence alignment computer programs, some sequence identity with known proteins were revealed.

PRO126

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1265 (shown in Figure 50 and SEQ ID NO:84) has certain amino acid sequence identity with the Fig1 polypeptide designated "MMUT/0429_1" in the Dayhoff database (version 35.45 Switstbrot 35).

O Accordingly, it is presently believed that PRO1265 disclosed in the present application is a newly identified member of the FIG1 family and may possess activity typical of the FIG1 polypeptide, including activation by intertentified.

PRO1250

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1250 (shown in Figure 52 and SEQ ID NO:86) has certain amino acid sequence identity with the human long chain fatty acid CoA ligase protein (LCFB_HUMAN). Accordingly, it is presently believed that PRO1250 disclosed in the present application is a newly identified long chain fatty acid CoA ligase homolog that may have activity typical of long chain fatty acis CoA ligase.

27. PRO1475

Using the WU-BLAST3 sequence alignment computer program, it has been found that a full-length native sequence PRO1475 (shown in Figure 54 and SEQ ID NO:88) has certain amino acid sequence identity with a portion of the mouse alpha-3-D-mannoside beat-1,2-N-acetylglucosaminyltransferase i protein.

25 Accordingly, it is presently believed that PRO1475 disclosed in the present application is a newly identified member of the N-acetylglucosaminyltransferase protein family and may possess activity typical of that protein family.

PRO137

As described herein, WU-BLAST2 sequence alignment computer programs were used to determine the sequence identity of the PRO1377 amino acid sequence with the amino acid sequences of known proteins. While some sequence identities were revealed, they were determined to not be significant. Accordingly, as far as it known, the DNA61608 sequence encodes a novel transmembrane protein designated berein as PRO1377.

29. PRO1326

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The DNA62808-1582 clone is believed to encode a secreted factor. As far as is known, the DNA62808-1582 sequence encodes a novel factor designated herein as PRO 1326; using WU-BLAST2 sequence alignment

computer programs, sequence identities to known proteins were revealed but determined not to be significant

. PRO124

The DNA62809-1531 clone was isolated from a human colon numor tissue library using a trapping occhaique which selects for nucleotide sequences encoding secreted proteins. As far as is known, the DNA62809-1531 sequence encodes a nowel factor designated herein as PRO1249, using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

i. KOISI

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length

10 native sequence PRO1315 (shown in Figure 62 and SEQ ID NO:104) has certain amino neid sequence identity
with the class II cytokine receptor 4 protein of mus musculus (MMU33696, 1). Accordingly, it is presently
believed that PRO1315 disclosed in the present application is a newly identified member of the cytokine receptor
protein family and may possess activity typical of that family.

15 32. PRO1599

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length mative sequence PRO1599 (shown in Figure 64 and SEQ ID NO:111) has certain amino axid sequence identity with Dayborff sequence "CFAD_PIG". Accordingly, it is presently believed that PRO1599 disclosed in the present application is a newly identified member of the Granzyme M family and may possess activity or properties typical of the Granzyme M family.

33. PRO143

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1430 (abown in Figure 66 and SEQ ID NO:116) has certain amino acid sequence identity prostate specific reductase (designated *P_W03198* in the Dayhoff database). Accordingly, it is presently believed that PRO1430 disclosed in the present application is a newly identified member of the reductase family and may possess activity typical of members of the reductase family.

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PRO1374

As far as is known, the DNA64849-1604 sequence encodes a novel factor designated herein as PRO1374; using WU-BLAST7 sequence alignment computer programs, some sequence identifies to known proteins such as the human alpha subunit of P4HA were revealed. Therefore, it is believed that PRO1374 is related to P4HA and may share one or more mechanisms.

35. PRO1311

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The DNA64863-1573 clone was isolated from human aortic endothelial cells and is believed to encode a novel transmembrane polypeptide designated herein as PRO1311. Using WU-BLAST2 sequence alignment

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computer programs; some sequence identities with known proteins were revealed, but were determined to not be significant.

36. PRO135

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1357 (shown in Figure 72 and SEQ ID NO:128) has certain amino acid sequence identity with the von Ebner minor salivary gland protein of mus musculus (MMU46068_1). Accordingly, it is presently believed that PRO1337 disclosed in the present application is a newly identified von Ebner minor salivary gland protein homolog.

10 37. PRO1244

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1244 (shown in Figure 74 and SEQ ID NO.130) has certain amino acid sequence identity with a known implantation-associated protein designated "AFQ08554, 1" on the Dnyhoff database (version 35.45 SwissProt 35). Accordingly, it is presently believed that PRO1244 disclosed in the present application is a newly 15 identified member of the implantation-associated protein family and may possess attachment activity typical of that protein family.

PRO1246

Using the WU-BLASTZ sequence alignment computer program, it has been found that a full-length
20 native sequence PRO1246 (shown in Figure 76 and SEQ ID NO:132) has certain amino acid sequence identity
with the murine bone-related subphatzes-like precursor protein (P_RS1335). Accordingly, it is presently believed
that PRO1246 disclosed in the present application is a newly identified bone-related sulphatzse homolog and may
possess activity typical of bone-related sulfatzse.

39. PRO1356

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Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1336 (shown in Figure 78 and SEQ ID NO:134) has certain amino acid sequence identity with the CPE-receptor protein of mus musculus (AB000713_1). Accordingly, it is presently believed that PRO1356 disclosed in the present application is a newly identified member of the CPE receptor family and may

30 possess activity typical of that family.

10. PRO1275

As far as is known, the DNA64888-1542 sequence encodes a novel factor designated herein as PRO1275. Using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

PROIZ74

As far as is known, the DNA64889-1541 sequence encodes a novel factor designated herein as PRO1274. Using WU-BLASTZ sequence alignment computer programs, some sequence identities to known proteins were revealed.

42. PRO1412

The DNA64897-1628 clome is believed to be a secreted factor. As far as is known, the DNA64897-1628 sequence encodes a novel factor designated berein as PRO1412; using WU-BLAST2 sequence alignment computer programs, sequence identities to known proteins were revealed but determined not to be significant.

10 43. PRO1557

Using WU-BLAST2 requence alignment computer programs, it has been found that a full-length native sequence PRO1557 (abown in Figure 86; SEQ ID NO:142) has certain amino acid sequence identity chordin protein designated AF034606_1 in the Dayhoff database. Accordingly, it is presently believed than PRO1557 disclosed in the present application is a newly identified member of the chordin family and may possess activity typical of the chordin family.

M. PKOJZ86

The DNA64903-1553 clone identified using techniques which selects for nucleotide sequences encoding secreted proteins. As far as is known, the DNA64903 sequence encodes a novel secreted factor designated herein as PRO1286. Using WU-BLAST2 sequence alignment computer programs, some sequence identifies to known proteins were revealed; however, it was determined that they were not significant.

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5. PRO1294

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length
25 native sequence PRO1294 (shown in Figure 90 and SEQ ID NO:146) has certain amino acid sequence identity
with the neuronal olfactomedin-related ER localized protein of the rat (173636). Accordingly, it is presently
believed that PRO1294 disclosed in the present application is a newly identified olfactomedin homolog and may
possess activity typical of that protein.

46. PRO1347

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1347 (shown in Figure 92 and SEQ ID NO:148) has certain amino acid sequence identity with butyrophilin. Moreover, there is a transmembrane domain approximately in the middle of the sequence as is typical of butyrophilins. Accordingly, it is presently believed that PRO1347 disclosed in the present application is a newly identified member of the butyrophilin family and may play a role in the budding and release of milk-fut glubules during lacention.

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7. PRO1305

The DNA66952-1508 clone was isolated from a human fetal kidney library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA64952-1508 clone does encode a secreted factor. As far as is known, the DNA64952 1508 sequence encodes a novel factor designated herein as PRO1305; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

· BROIZE

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1273 (abown in Figure 96 and SEQ ID NO:158) has certain amino acid sequence identity with a [0] lipocalin precursor. Moreover, Figure 96 ahows that PRO1273 has a motif conserved in lipocalins. Accordingly, it is presently believed that PRO1273 disclosed in the present application is a newly identified member of the lipocalin family and shares at least one mechanism with lipocalins.

PRO1302

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1302 (shown in Figure 98 and SEQ ID NO:160) has certain amino acid sequence identity with CD33L1 and CD33L2. Accordingly, it is presently believed that PRO1302 disclosed in the present application is a newly identified member of the sialoudhesin family and possesses characteristics typical of this family. Specifically, PR01302 may be involved in cancer, inflammation, hemopoisis, neuronal development and/or 20 immunity.

50. PRO1283

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-tength native sequence PRO1283 (shown in Figure 100 and SEQ ID NO:162) has certain amino acid sequence identity 25 with the rat odorant binding protein homolog OBP-II precursor (A40464). Accordingly, it is presently believed that PRO1283 disclosed in the present application is a newly odorant binding protein and may possess activity typical of the odorant binding proteins.

PRO1279

30 Using the WU-BLAST2 acquence alignment computer program, it has been found that a full-length native sequence PRO1279 (shown in Figure 102 and SEQ ID NO:170) has certain amino acid sequence identity with the mouse narropsin protein (156359). Accordingly, it is presently believed that PRO1279 disclosed in the present application is a newly identified neuropsin homolog and may possess activity typical of the neuropsin protein.

52. PRO1304

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Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length

native sequence PRO1304 (shown in Figure 104 and SEQ ID NO: 180) has certain amino acid sequence identity with the FK-506 binding protein of mus musculus (AFN40252_I). Accordingly, it is presently believed that PRO1304 disclosed in the present application is a newly identified member of the FK506 binding protein family and may powers activity typical of that family.

S3. PRO1317

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1317 (shown in Figure 106 and SEQ ID NO:189) has certain amino acid sequence identity with human CD97 protein. Accordingly, it is presently believed that PRO1317 disclosed in the present application is a leuthocyte antigen that may be involved in leukocyte activation.

54. PRO130

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1303 (shown in Figure 108 and SEQ ID NO:194) has certain amino acid sequence identity with neuropsin. Accordingly, it is presently believed that PRO1303 disclosed in the present application is a newly identified member of the serine protease family and may possess catabolic activity typical of this family.

S. PROLIG

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1306 (shown in Figure 110 and SEQ ID NO:196) has certain amino acid sequence identity with 20 Dayhorf sequence no. AIF1_HUMAN. Accordingly, it is presently believed that PRO1306 disclosed in the present application is a newly identified member of the AIF1/daintain family and may possess activity and properties typical of AIF1/daintain.

56. PRO133

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1336 (shown in Figure 112 and SEQ ID NO:198) has certain amino acid sequence identity with alit. Accordingly, it is presently believed that PRO1336 disclosed in the present application is a newly identified member of the EGF-repeat family and may possess protein interaction mediation activity.

57. PRO1278

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1278 (shown in Figure 114 and SEQ ID NO:203) has certain amino acid sequence identity bysozyme c -1 precursor designated "LYCL_ANAPL" in the Dayhoff database. Accordingly, it is presently believed that PRO1278 disclosed in the present application is a newly identified member of the lysozyme family and may possess bydrolytic and other activity typical of the lysozyme family.

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58. PRO1298

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1298 (shown in Figure 116 and SEQ ID NO.210) has certain amino acid sequence identity with glycosyltransferase alg2. Accordingly, it is presently believed that PRO1298 disclosed in the present application is a newly identified member of the glycosyltransferase family and may share at least one mechanism with members of this family.

PROLIDI

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1301 (shown in Figure 118 and SEQ ID NO:212) has consistent amino acid sequence identity with 10 cytochrome P450 proteins. Accordingly, it is presently believed that PRO1301 disclosed in the present application is a newly identified member of the cytochrome P450 family and may possess monooxygenase activity typical of the cytochrome P450 family.

PRO1268

As far as is known, the DNA66519-1535 sequence excedes a tovel transmembrane polypeptide factor designated herein as PRO1268. Using WU-BLAST2 sequence alignment computer programs, sequence identity to a known protein was revealed, but determined to not be significant.

il. PRO1269

20 Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1269 (abown in Figure 122 and SEQ ID NO:216) has certain amino acid sequence identity a bovine granulocyte peptide A precursor, designated "P_W23722" on the Dayhoff database (version 35.45 SwissProt 35). Accordingly, it is presently believed that PRO1269 disclosed in the present application is a newly identified member of the granulocyte A peptide family and may possess microbial activity typical of that family 25 of peptides.

2. PRO132

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1327 (shown in Figure 124 and SEQ ID NO:218) has certain amino acid sequence identity 30 with the rat neurocophilin-I protein (NPHI_RAT). Accordingly, it is presently believed that PRO1327 disclosed in the present application is a newly identified member of the neurocophilin protein family and may possess activity typical of that protein family.

5. PRO1382

35 Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1382 (shown in Figure 126 and SEQ ID NO:220) has certain amino acid sequence identity with the amino acid sequence of a known cerebellin-like glycoprotein designated "CERL_RAT" in the Dayhoff

dambase. Accordingly, it is presently believed that PRO1382 disclosed in the present application is a newly identified member of the cerebellin family of neuropoptides and may possess activity and properties typical of cerebellin.

64. PRO1328

The DNA66658-1584 clone was isolated from a human diseased prostate tissue library using a trapping technique which selects for nucleoxide sequences encoding proteins. As far as is known, the DNA66658-1584 sequence encodes a novel factor designated herein as PRO1328; using the WU-BLAS72 sequence alignment computer program, no significant sequence identities to any known proteins were revealed.

10 65. PRO1325

The DNA66659-1593 clone was isolated from a human thymus tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA66659-1593 sequence encodes a novel factor designated herein as PRO1325; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

s. PRO13

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1340 (shown in Figure 132 and SEQ ID NO:229) has certain amino acid sequence identity with Dayhoff sequence no. 146336. Accordingly, it is presently believed that PRO1340 disclosed in the present application is a newly identified member of the cadherin family and may possess activity and properlies typical of the cadherin family.

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7. PRO1339

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native
25 sequence PRO1339 (shown in Figure 134 and SEQ ID NO:234) has certain amino acid sequence identity with
human pancreatic carboxypepidase and carboxypepidase al. Accordingly, it is presently believed that
PRO1339 disclosed in the present application is a newly identified member of the carboxypepidase family and
possesses caboxypepidase activity.

68. PRO1337

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1337 (abown in Figure 136 and SFQ ID NO:236) has certain amino acid sequence identity with a human TBG identified as "THBG_HUMAN" in the Dayhoff database. Accordingly, it is presently believed that PRO1337 disclosed in the present application is a newly identified member of the TBG family and may possess thyroid hormone transport capability and have other

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59. PRO1342

The DNA66674-1599 clone was isolated from human crophageal tissue. As described in further detail below, using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed. The DNA66674-1599 clone appears to encode for a novel transmembrane pulypepide.

70. PRO134

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The DNA66675-1587 clone was isolated from a human smooth muscle cell tissue library using a trapping technique which selecus for nucleotide sequences encoding secreted proteins. Thus, the DNA66675-1587 clone does encode a secreteal factor. As far as Is known, the DNA66675-1587 sequence encodes a novel factor designated herein as PRO1343; using the WU-BLAST2 sequence alignment computer program, no significant sequence identities to any known proteins were revealed.

71. PRO1480

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length narive requence PRO1480 (shown in Figure 142 and SEQ ID NO:253) has certain amino acid sequence identity with 15 Dayhoff sequence no. 148746. Accordingly, it is presently believed that PRO1480 disclosed in the present application is a newly identified member of the Semaphorin C family

72. PRO1487

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native
20 sequence PRO1487 (Figure 144; SEQ ID NO; 260) has certain amino acid sequence identity with a radical fringe
protein designated GGU82088_1 on the Daythoff database. Accordingly, it is presently believed that PRO1487
disclosed in the present application is a newly identified member of the fringe family and may possess activity
typical of the fringe family.

73. PRO1418

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As far as is known, the DNA68864-1629 sequence encodes a novel factor designated herein as PRO1418. Using WU-BLAST2 sequence alignment computer programs, sequence identifies to known proteins were minimal.

30 74. PRO1472

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1472 (shown in Figure 148 and SEQ ID NO:267) has certain amino acid sequence identity with hutyrophilin. Accordingly, it is presently believed that PRO1472 disclosed in the present application is a newly identified member of the butyrophilin family and may possess involvement in lactation.

75. PRO1461

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native

sequence PRO1461 (shown in Figure 150 and SEQ ID NO:269) has certain amino acid sequence identify the trypnin-like enzyme identified as "P_R89435" on the Dayhoff database. Accordingly, it is presently believed that PRO1461 disclosed in the present application is a newly identified member of the serine procease family and may possess serine procease activity, and more particularly, may possess enzymatic activity typical of other trypnin-like enzymes. Homology was also found to exist between the PRO1461 amino acid sequence and other trypnin-like enzymes and scrine proceases in the Dayhoff database.

e. EKUJAI

The DNA68874-1622 clone was isolated from a human brain meningiona tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA68874-1622 10 sequence encodes a novel factor designated herein as PRO1410; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

PRO156

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native 15 sequence PRO1568 (shown in Figure 154, and SEQ ID NO:273) has certain amino acid sequence identity to tetraspan 5 and tetraspan 4. Accordingly, it is presently believed that PRO1568 disclosed in the present application is a newly identified member of the tetraspanin family and may possess molecular facilitator activity typical of this family.

20 78. PRO1570

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1570 (abown in Figure 156 and SEQ ID NO:275) has certain amino acid sequence identity with SP60; however, for the first time, the first 199 amino acids (or amino terminal end) of that protein are identified and presented herein. Accordingly, it is presently believed that PRO1570 disclosed in the present application is a newly identified member of the scrine protease family and is involved in carcinoma.

9. PRO131

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1317 (shown in Figure 158 and SEQ ID NO.277) has certain amino acid sequence identity with 30 a known semaphorin B protein, designated "48745" on the Dayhoff database. Accordingly, it is presently believed that PRO1317 disclosed in the present application is a newly identified member of the semaphorin glycoprotein family and may possess activity or properties typical of semaphorins.

. PRO178

35 Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1780 (shown in Figure 160 and SEO ID NO:282) has certain amino acid sequence identity with a known glucumonosyltransferase designated "UDA2_RABIT" in the Dayboff database. Accordingly, it is

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presently believed that PRO1780 disclosed in the present application is a newly identified member of the gluctronosyltransferase family and may possess enzymatic activity and other properties typical of the gluctronosyltransferase family.

81. PRO1486

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1486 (shown in Figure 162 and SEQ ID NO-287) has certain amino acid sequence identity with cerebellin I precursor. Accordingly, it is presently believed that PRO1486 disclosed in the present application is a newly identified member of the cerebellin family and shares at least one mechanism with ocrebellin.

10 82. PRO143

The DNA71184-1634 clone was isolated from a human adrenal gland tissue library using a trapping technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA71184-1634 sequence encodes a novel factor designated tierein as PRO1433; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

83. PRO149

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Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1490 (shown in Figure 166 and SEQ ID NO:297) has certain amino acid sequence identity with a portion of the 1-acyl-sn-glycerol-3-phosphate acyltransferase protein (\$60478). Accordingly, it is presently believed that PRO1490 disclosed in the present application is a newly identified member of the acyltransferase protein family and may possess activity typical of 1-acyl-an-glycerol-3-phosphate acyltransferase proteins.

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PRO1482

The DNA71234-1651 clone was isolated from a human adrenal gland library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the DNA71234-1651 clone does encode a secreted factor. As far as is known, the DNA71234-1651 sequence encodes a novel factor designated herein as PRO1482; using the WU-BLAST2 sequence alignment computer program, no sequence identities to any known proteins were revealed.

85. PRO14

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As far as is known, the DNA71277-1636 sequence encodes a novel factor designated herein as PRO1446. Using WU-BLAST2 sequence alignment computer programs, minimal sequence identities to known proteins were revealed.

86. PRO1558

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Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length

native sequence PRO1558 (shown in Figure 172 and SEQ ID NO:306) has significant amino acid sequence identity with a methyltransferase protein (CAMT_EUCGU). Accordingly, it is presently believed that PRO1558 disclosed in the present application is a newly identified member of the methyltransferase protein family and may possess activity typical of that provein family.

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length narive sequence PRO1604 (shown in Figure 174 and SEQ ID NO;308) has certain unitio acid sequence identity with the mouse liver cancer-originated cell growth factor designated P_W37483 on the Dayhoff database. Accordingly, it is presently believed that PRO1604 disclosed in the present application is a newly identified member of the HDGF family and may possess growth factor activity typical of other HDGFs.

PR0149

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1491 (shown in Figure 176 and SEQ ID NO:310) has certain amino acid

15 sequence identity with a portion of the collupsin-2 protein of Gallus gallus (GGUZ8240_1). Accordingly, it is presently believed that PRO1491 disclored in the present application is a newly identified member of the collupsin protein family and may possess activity typical of that protein family.

89. PRO143

20 It has been found that the full-length native sequence PRO1431 [abown in Figure 178 (SEQ ID NO:315) has significant sequence identity with the SH3 domain comaining protein SH17_HUMAN. Accordingly, it is presently believed that PRO1431 disclosed in the present application is a newly identified member of proteins having an SH3 domains and may possess signal transduction properties.

90. PRO1563

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Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of a full-length native sequence PRO1563 (shown in Figure 180 and SEQ ID NO:317) has certain amino acid sequence identity with a portion of the mouse ADAMTS-1 protein (AB001735_1). Accordingly, it is presently believed that PRO1563 disclosed in the present application is a newly identified member of the ADAM protein family and may possess activity typical of that protein family.

PRO1565

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Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1565 (shown in Figure 182 and SEQ ID NO:322) has certain amino acid

35 sequence identity with a portion of the chondromodulin-I protein of ratus norvegicus (APO51425_1).

Accordingly, it is presently believed that PRO1565 disclosed in the present application is a newly identified member of the chondromodulin protein family and may possess activity typical of that protein family.

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Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1571 (shown in Figure 184 and SEQ ID NO:324) has certain amino acid sequence identity with a portion of the human clostridium perfringens emerotoxia receptor protein (AB000712_1). Accordingly, it is presently believed that PRO1571 disclosed in the present application is a newly identified CPE-R homolog and may possess activity typical of the CPE-R protein.

93. PRO1572

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1572 (shown in Figure 186 and SEQ ID NO:326) has certain amino acid sequence identity with CPB-R. Accordingly, it is presently believed that PRO1572 disclosed in the present application is related to CPB-R and may possess at least one shared mechanism.

PRO1573

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native

15 sequence PRO1573 (shown in Figure 188 and SEQ ID NO:328) has certain amino acid sequence Identity with

CPE-R. Accordingly, it is presently believed that PRO1573 disclosed in the present application is related to

CPE-R and may possesses at least one shared mechanism.

5. PRO1488

20 Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1488 (Figure 190; SEQ ID NO:330) has certain amino acid sequence identity with a known CPE-R designated *AB000712_1* on the Dayhoff database. Accordingly, it is presently believed that PRO1488 disclosed in the present application is a newly identified member of the CPE-R family and may possess binding activity typical of the CPE-R family.

5. PRO14

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Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1489 (shown in Figure 192 and SEQ ID NO:332) has certain amino acid sequence identity with the clostridium perfringens enterotoxin receptor of Cercopitheous aethiops (D88492_1).

30 Accordingly, it is presently believed that PRO1489 disclosed in the present application is a newly identified clostridium perfringens enterotoxin receptor homolog and may possess activity typical of the clostridium perfringens enterotoxin receptor protein.

97. PRO1474

35 Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1474 (shown in Figure 194 and SEQ ID NO:334) has certain amino acid sequence identity with ovonnucoid. Accordingly, it is presently believed that PRO1474 disclosed in the present application is a newly

identified member of the kazal serine protesse inhibitor family and may possess serine protesse inhibitory activity typical of this family.

PRO150

The DNA73742-1508 clone was isolated from a human diseased cartilage fistue library. As far as is 5 known, the DNA73742-1508 sequence emerdes a novel factor designated herein as PRO1508; although, using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

9. PRO155

O The DNA73744-1665 clone was isolated from a human tissue library. As far as is known, the DNA73744 sequence encodes a novel transmembrane protein designated herein as PRO1555. Using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

00. PRO148

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1485 (shown in Figure 200 and SEQ ID NO:340) has certain amino acid sequence identity with lystayme C precursor peptide. Accordingly, it is presently believed that PRO1485 disclosed in the present application is a newly identified member of the lystayme family and shares at least one like mechanism.

20 101. PRO1564

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of a full-length native sequence PRO1564 (shown in Figure 202 and SEQ ID NO:347) has certain amino acid sequence identity with a portion of a mouse polypeptide GalNAc transferase T4 protein (MMU73819_1). Accordingly, it is presently believed that PRO1564 disclosed in the present application is a newly identified member of the N-acetylgalactosaminyltransferase protein family and may possess activity typical of that protein family.

102. PRO1755

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As far as is known, the DNA76396-1698 sequence encodes a novel transmembrane protein designated
30 herein as PRO1755. Although, some sequence identities to known proteins was revealed using WU-BLAST2
sequence alignment computer programs.

PK01757

The DNA76398-1699 clone was isolated from a human testicular tissue library using a trapping 35 technique which selects for nucleotide sequences encoding proteins. As far as is known, the DNA76398-1699 sequence encodes a novel factor designated herein as PRO1757; using the WU-BLAST2 sequence alignment computer program, no significant requence identities to any known proteins were revealed.

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104. PRO175

The DNA76399-1700 clone was isolated from a library derived from human thymus tissue obtained from a fetus that died at 17 weeks' gestation from aneurophalus. It is believed that the DNA76399-1700 clone encodes a novel secreted factor, designated herein as PRO1758. Using WU-BLAST2 sequence alignment computer programs, significant sequence identity was revealed between the amino acid sequences of PRO1758 and Dayboff sequence No. AC005328_2.

s. - PRO1575

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Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1575 (abown in Figure 210 and SEQ ID NO:358) has certain amino acid sequence identity with 10 Dayhoff sequence no. A12005_1. Accordingly, it is presently believed that PRO1575 disclosed in the present applituation is a newly identified member of the protein distified isomerase family and may possess activity and properties typical of the distified isomerase family.

PRO1787

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native requence PRO1787 (shown in Figure 212 and SEQ ID NO:364) has certain amino acid sequence identity with various species of myelin p0. Accordingly, it is presently believed that PRO1787 disclosed in the present application is a newly identified member of the myelin p0 protein family and may share at least one similar mechanism. It is believed that modulators of PRO1787 may be used to reas myelin p0 associated disorders, such 20 as neuropathy, hereditary tooth disease, etc.

107. PRO1781

Using WU-BLAST2 sequence alignment computer programs, some sequence identities were found between the PRO1781 amino acid sequence (SEQ ID NO:366) and the amino acid sequences of known proteins, 25 but were not found to be significant. Accordingly, as far as is known, the DNA76522-2500 sequence encodes a novel protein.

108. PRO1556

The DNA76529-1666 clone was isolated from a human breast tumor tissue library. As far as is known, 30 the DNA76529-1666 sequence encodes a novel transmembrane protein designated herein as PRO1556. Using WU-BLASTZ sequence alignment computer programs, some sequence identifies to known proteins were revealed.

y. PKO1759

35 As far as is known, the DNA76531-1701 sequence encodes a movel factor designated herein as PRO1759; using WU-BLAST2 sequence alignment computer programs, limited sequence identities to known proteins were revealed.

110. PRO1760

As far as is known, the DNA76532-1702 sequence encodes a novel factor designated herein as PRO1760; using WU-BLAST2 sequence alignment computer programs, limited sequence identities to known proteins were revealed.

5 111. PRO1561

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of a full-length native sequence PRO1561 (shown in Figure 222 and SEQ ID NO:578) has certain amino acid sequence identity with a portion of the human phospholipase A2 protein (P_R63053). Accordingly, it is presently believed that PRO1561 disclosed in the present application is a newly identified member of the phospholipase A2 protein family and may possess activity typical of that protein family.

PRO156;

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Using WU-BLASTZ sequence alignment computer programs, it has been found that a full-length native sequence PRO1567 (Figure 224; SEQ ID NO:383) has certain amino acid sequence identity with human colon specific gene CSG6 polypeptide, identified as P_W0549 on the Dayhoff database. Accordingly, it is presently believed that PRO1567 disclosed in the present application is a newly identified CSG expression product, and may possess properties typical of such proteins.

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13. PRO169.

20 Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1693 (shown in Figure 226 and SEQ ID NO.385) has certain amino acid sequence identity with a portion of a mouse insulin-like growth factor binding protein (ALS_MOUSE). Accordingly, it is presently believed that PRO1693 disclosed in the present application is a newly identified member of the insulin-like growth factor binding protein family and may possess activity typical of that protein family.

4. PRO17

As far as is known, the DNA77303-2502 sequence encodes a novel factor designated herein as PRO1784; using WU-BLAST2 sequence alignment computer programs, some sequence identities to known proteins were revealed.

5. PRO1605

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Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1605 (shown in Figure 230 and SEQ ID NO.395) has certain amino acid sequence identity with a portion of the human alpha-1,3-mannosylglycoproucin beta-1,6-n-accyltransferase protein (GNTS_HUMAN). Accordingly, it is presently believed that PRO1605 disclosed in the present application is a newly identified member of the glycosyltransferase protein family and may possess activity

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typical of that protein family.

116. PRO1788

Using WU-BLAST2 sequence alignment computer programs, it has been found that a full-length native sequence PRO1788 (shown in Figure 232 and SEQ ID NO:397) has certain amino acid sequence identity with Dayboff sequence "GARP_HUMAN", a leucine-rich repest-containing protein encoded by a gene localized in the 11q14 chromosomal region. Accordingly, it is presently believed that PRO1788 disclosed in the present application is a newly identified member of the leucine-rich repeat-containing family and may possess activity or properties typical of the leucine-rich repeat-containing family.

10 117. PRO180

Using the WU-BLAST2 sequence alignment computer program, it has been found that a portion of the full-length native sequence PRO1801 (shown in Figure 234 and SEQ ID NO:402) has certain amino acid sequence identity with a portion of the IL-19 protein (P_W37935). Accordingly, it is presently believed that PRO1801 disclosed in the present application is a newly identified member of the IL-10-related cytokine family and may possess activity typical of that cytokine family.

UCP4

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Using the Megalign DNASTAR computer program (and algorithms and parameters in this software set by the manufacturer) (Oxford Molecular Group, Inc.), it has been found that a full-length native sequence UCP4 (abown in Figure 236 and SEQ ID NO:406) has certain amino acid sequence identity with UCP3, UCP2 and UCP1. Accordingly, it is presently believed that UCP4 disclosed in the present application is a newly identified member of the human uncoupling protein family and may possess activity(s) and/or property(s) ypical of that protein family, such as the ability to enhance or supress metabolic rate by affecting mitochondrial membrane potential.

119. PRO193

The present invention provides newly identified and tooland nucleotide sequences emoding polypopides referred to in the present application as PRO193. In particular, Applicants have identified and isolated cDNA encoding a PRO193 polypoptide, as disclosed in further detail in the Examples below. The PRO193-encoding

clone was isolated from a human retina library.

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20. PRO1130

Using the WU-BLASTZ sequence alignment computer program, it has been found that a full-length native sequence PRO1130 (shown in Figure 240 and SEQ ID NO:415) has amino acid sequence identity with 35 the human 2-19 protein. Accordingly, it is presently believed that PRO1130 disclosed in the present application is a newly identified 2-19 protein homolog.

PRO1335

5 family and may possess activity typical of that family. PRO1335 disclosed in the present application is a newly identified member of the carbonic anhydrase protein with the human carbonic authydrase precursor protein (AF037335_1). Accordingly, it is presently believed that native sequence PRO1335 (shown in Figure 242 and SEQ ID NO:423) has certain amino acid sequence identity Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length

computer programs, requence identities to known proteins were revealed but determined not to be significant 1585 sequence encodes a novel factor designated herein as PRO1329; using WU-BLAST2 sequence alignment The DNA66660-1585 clone is believed to encode a secreted factor. As far as is known, the DNA66660-

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BLAST2 sequence alignment computer programs, sequence identities to known proteins were revealed but as is known, the DNA76393-1664 sequence encodes a novel factor designated herein as PRO1550; using WUdetermined not to be significant. The DNA76393-1664 clone was isolated from a subtracted human breast numor tissue library. As far

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20 the PRO DNA, and/or by synthesis of the desired PRO polypeptide. Those skilled in the art will appreciate that PRO variants can be prepared. PRO variants can be prepared by introducing appropriate nucleotide changes into of glycosylation sites or altering the membrane anchoring characteristics. amino sold changes may alter post-translational processes of the PRO, such as changing the number or position In addition to the full-length native sequence PRO polypeptides described berein, it is contemplated that

ઝ 25 amino acid residue may he inserted, substituted or deleted without adversely affecting the desired activity may replacements. Insertions or deletions may optionally be in the range of about 1 to 5 amino acids. The variation be found by comparing the sequence of the PRO with that of homologous known protein molecules and PRO as compared with the native sequence PRO. Optionally the variation is by substitution of at least one amino can be made, for example, using any of the techniques and guidelines for conservative and non-conservative and/or obstructly properties, such as the replacement of a leucine with a serine, i.e., conservative amino acid minimizing the number of amino acid sequence changes made in regions of high homology. Amino acid acid with any other antino acid in one or more of the domains of the PRO. Guidance in determining which insertion of one or more codons encoding the PRO that results in a change in the amino acid sequence of the mutations set forth, for instance, in U.S. Patent No. 5,364,934. Variations may be a substitution, deletion or sequence and testing the resulting variants for activity exhibited by the full-length or mature native sequence allowed may be determined by systematically making inscritons, deletions or substitutions of amino acids in the substitutions can be the result of replacing one amino acid with another amino ocid having similar structural Variations in the native full-length sequence PRO or in various domains of the PRO described herein,

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Certain fragments lack amino acid residues that are not essential for a desired biological activity of the PRO or C-terminus, or may lack internal residues, for example, when compared with a full length native protein. PRO polypeptide fragments are provided herein. Such fragments may be truncated at the N-terminus

5 v termini of the DNA fragment are employed at the 5' and 3' primers in the PCR. Preferably, PRO polypeptide fragments may be chemically synthesized. An alternative approach involves generating PRO fragments by fragments share at least one hiological and/or immunological activity with the native PRO polypeptide disclosed a desired polypeptide fragment, by polymerase chain reaction (PCR). Oligonucleotides that define the desired desired fragment. Yet another sultable technique involves isolating and amplifying a DNA fragment encoding particular amino acid residues, or by digesting the DNA with suitable restriction enzymes and isolating the enzymatic digestion, e.g., by treating the protein with an enzyme known to cleave proteins at sites defined by PRO fragments may be prepared by any of a number of conventional techniques. Desired peptide

15 changes, denominated exemplary substitutions in Table 1, or as further described below in reference to amino of preferred substitutions. If such substitutions result in a change in biological activity, then more substantial acid classes, are introduced and the products screened. In particular embodiments, conservative substitutions of interest are shown in Table 1 under the heading

	(V)	yr (Y)	(%)	3	Ser (S)	Pro (P)	Phe (F)	Met (M)	Lys (K)		Leu (L)		Ile (I)	His (H)	Gly (G)	Gh (E)	Ch (Q)	လှူး (C)	Asp (D)	Asn (N)	Arg (R)	Ala (A)	Residue	Original	
ala; norleucine	ile; leu; met; phe;	trp: phe; thr; ser	iye; phe	ser	2	aia	leu; val; ile; ala; tyr	leu; phe; ile	arg; gtn; asn	met; ala; phe	noriescine; ile; val;	norleucine	ieu; val; met; ala; phe;	asn; gln; lys; arg	pro; ala	asp	asn	Ser	glu	gln; his; tys; arg	lys; gh; asn	val; leu; ile	Substitutions	Exemplary	Table 1
leu		pie	yr.	ser	Ē	ala	leu	F.	2/2	ile		leu		Sire	ala	asp	asn	Ser	glu	gh.	łys	val	Substitutions	Preferred	

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Substantial modifications in function or immunologicalidentity of the PRO polypeptide are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Naturally occurring residues are divided into groups based on common side-chain properties:

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(1) hydrophobic: norleucine, met, ala, val, leu, ile;

(2) neural hydrophilic: cys, ser, thr;

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scius: asp. giu;

(4) basic: asn, gln, his, lys, arg;

(5) residues that influence chain orientation: gly, pro; and

(6) aromatic: up, tyr, phe.

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Non-conservative substitutions will entail exchanging a member of one of these classes for another class. Such substituted testitues also may be introduced into the conservative substitution sites or, more preferably, into the remaining (non-conserved) sites.

The variations can be made using methods known in the art such as oligonucleotide-mediated (size-directed) mutagenesis, alarine scanning, and PCR mutagenesis. Size-directed mutagenesis [Carter et al., Nucl. Acids Res., 12:6487 (1987)], cassette mutagenesis [Wells et al., Cente., 24:315 (1985)], restriction selection mutagenesis [Wells et al., Philos. Trans. R. Soc. London SetA. 312:415 (1986)] or other known techniques can be performed on the cloned DNA to produce the PRO variant

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DNA.

Scanning amino acid analysis can also be employed to identify one or more amino acids along a contiguous sequence. Among the preferred scanning amino acids are relatively small, neutral amino acids. Such amino acids include atanine, glycine, serine, and cysteine. Alanine is typically a preferred scanning amino acid among this group because it eliminates the side-chain beyond the beta-carbon and is less likely to alter the mainschain conformation of the variant [Cunningham and Wells, Science, 244: 1081-1085 (1989)]. Alanine is also typically preferred because it is the most common amino acid. Further, it is frequently found in both buried and exposed positions [Creighon, The Proteins, (W.H. Freeman & Co., N.Y.); Chothis, <u>1. Mol., Biol.</u>, 150: (1976)]. If alanine substitution does not yield adequate amounts of variam, an isoteric amino acid can be used.

C. Modifications of PRO

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Covalent modifications of PRO are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a PRO polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N- or C- terminal residues of the PRO. Derivatization with hifunctional agents is useful, for instance, for crosslinking PRO to a water-insoluble support matrix or surface for use in the method for purifying anti-PRO antibodies, and vice-versa. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacety)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidorsters, including disuccinimidy testers such as 3,3'-dihinobis(succinimidy)tpropionate), bifunctional maleimiders such as bis-N-maleimido-1,8-octane and agents such as methyl-3-{(p-azidophenyl)dithio)propioimidate.

Other modifications include deamidation of glutaminyl and asparaginyl residues to the corresponding glutamyl and asparayl residues, respectively, bydroxylation of proline and lysine, phosphorylation of hydroxylation of seryl or threonyl residues, methylation of the a amino groups of tysine, arginine, and histoidine side chains [T.E. Creighton, Proteins: Structure and Molecular Protecties, W.H. Freeman & Co., San Francisco, pp. 79-86 (1983)], accytation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

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Another type of covalent modification of the PRO polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Aftering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence PRO (either by removing the underlying glycosylation site or by deleting the glycosylation by chemical and/or emzymatic means), and/or adding one or more glycosylation sites that are not present in the native sequence PRO. In addition, the phrase includes qualitative changes in the glycosylation of the native proteins, involving a change in the nature and proportions of the various carbohydrate moieties present.

Addition of glycosylation sites to the PRO polypeptide may be accomplished by altering the amino acid sequence. The alteration may be made, for example, by the addition of, or substitution by, one or more serine or threomine residues to the native sequence PRO (tor O-linked glycusylation sites). The PRO amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the PRO polypeptide at preschetted bases such that codors are generated that will translate into the desired amino acids.

in WO 87/05330 published 11 September 1987, and in Aplin and Wriston, CRC Crit. Rev. Biochem., pp. 259chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., Another means of increasing the number of carbohydrate moieties on the PRO polypeptide is by

- or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets of endo- and exo-glycosidases as described by Thotakura et al., Meth. Enzymol., 138:350 (1987). (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety Hakimuddin, et al., Arch. Biochem. Biophys., 252:52 (1987) and by Edge et al., Anal. Biochem., 118:131 for glycosylation. Chemical deglycosylation techniques are known in the art and described, for instance, by Removal of carbohydrate moieties present on the PRO polypeptide may be accomplished chemically
- the manner set forth in U.S. Patent Nos. 4,640.835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337 of nonproceinanceous polymets, e.g., polyethylene glycol (PEG), polypropylene glycol, or polyoxyalkylenes, in Another type of covalent modification of PRO comprises linking the PRO polypeptide to one of a variety

comprising PRO fused to another, heterologous polypeptide or amino acid sequence. The PRO of the present invention may also be modified in a way to form a chimeric molecule

- 25 20 15 553 (1990)]. Other tag polypeptides include the Flag-peptide [Hopp et al., BioTechnology, 6:1204-1210 to the eprimpe tag. Various tag polypeptides and their respective amibodies are well known in the art. Examples (1988)]; the KT3 epitope peptide [Martin et al., Science, 255:192-194 (1992)]; an a-tubulin epitope peptide G4, B7 and 9E10 antibodies thereto [Evan et al., Molecular and Cellular Biology, 5:3610-3616 (1985)]; and the [Skinner et al., L.Biol. Chem., 266:15163-15166 (1991)]; and the T7 gene 10 protein peptide tag [Lutz Freyermuth et al., Proc. Natl. Acad. Sci. USA, 82:6393-6397 (1990)]. Herpes Simplex virus glycoprotein D (gD) tag and its antibody [Paborsky et al., Protein Engineering, 2(6):547. antibody 12CA5 [Field et al., Mol. Cell. Biol., 8:2159-2165 (1988)]; the c-myc tag and the 8F9, 3C7, 6E10, include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; the flu HA tag polypeptide and its be readily purified by affinity purification using an anti-tag antibody or another type of affinity matrix that binds detected using an ambody agains the tag polypeptide. Also, provision of the epitope tag enables the PRO to at the amino- or carboxyl- terminus of the PRO. The presence of such epitope-tagged forms of the PRO can be which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed In one embodiment, such a chimeric molecule comprises a fusion of the PRO with a tag polypeptide
- 35 30 regions of an IgG1 molecule. For the production of immunoglobulin fusions see also US Petent No. 5,428,130 immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule (also referred to as an "immunoadhesin"), such a fusion could be to the Fe region of an IgG molecule. The Ig fissions polypeptide in place of at least one variable region within an Ig molecule. In a particularly preferred preferably include the substitution of a soluble (transmembrane domain deleted or inactivated) form of a PRO mbodiment, the immunoglobulin fusion includes the hinge, CH2 and CH3, or the hinge, CH1, CH2 and CH3 In an alternative embodiment, the chimeric molecule may comprise a fusion of the PRO with an

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D. Preparation of PRO

5 et al., Solid-Phase Peptide Synthesis, W. II. Freeman Co., San Francisco, CA (1969); Metrificid, L. Am. Chem. Synthesizer (Foster City, CA) using manufacturer's instructions. Various portions of the PRO may be chemically synthesized separately and combined using chemical or enzymatic methods to produce the full-length 80c., 85:2149-2154 (1963)]. In vitro protein synthesis may be performed using manual tochniques or by portions thereof, may be produced by direct peptide synthesis using solid-phase techniques (see, e.g., Stewart which are well known in the art, may be employed to prepare PRO. For instance, the PRO sequence, or transfected with a vector combining PRO nucleic acid. It is, of course, comemplated that alternative methods unomation. Automated synthesis may be accomplished, for instance, using an Applied Biosystems Peptide The description below relates primarily to production of PRO by culturing cells transformed or

Isolation of DNA Encoding PRO

7 obtained from a cDNA library prepared from human tissue, such as described in the Examples. The PRO nucleic acid symbesis). encoding gene may also be obtained from a genomic library or by known synthetic procedures (e.g., amomated the PRO mRNA and to express it at a detectable level. Accordingly, human PRO DNA can be conveniently DNA encoding PRO may be obtained from a cDNA library prepared from issue believed to possess

20 or genomic library with the selected probe may be conducted using standard procedures, such as described in supra; Dieffenbach et al., PCR Primer: A Laboratory Manual (Cold Spring Harbor Laboratory Press, 1995)] Sambrook et al., Molecular Cloning: A Laboratory Manual (New York: Cold Spring Harbor Laboratory Press about 20-80 bases) designed to identify the gene of interest or the protein encoded by it. Screening the cDNA 1989). An alternative means to isolate the gene emoding PRO is to use PCR methodology (Sambrook et al. Libraries can be screened with probes (such as antibodies to the PRO or oligonucleotides of at least

- 25 selected as probes should be of sufficient length and sufficiently unambiguous that false positives are minimized ATP, blothylation or enzyme labeling. Hybridization conditions, including moderate stringency and high being screened. Methods of labeling are well known in the art, and include the use of radiolabels like. #P-labeled The oligonucleotide is preferably labeled such that it can be detected upon hybridization to DNA in the library stringency, are provided in Sambrook et al., supra, The Examples below describe techniques for screening a cDNA library. The oligonucleotide sequences
- 30 the full-length sequence can be determined using methods known in the art and as described herein. Sequence identity (at either the amino acid or nucleotide tevel) within defined regions of the molecule or across sequences deposited and available in public databases such as GenBank or other private sequence databases Sequences identified in such library screening methods can be occupared and aligned to other known
- 35 libraries using the deduced amino acid sequence disclosed herein for the first time, and, if necessary, using conventional primer extension procedures as described in Sambrook et al., supra, to detect procursors and processing intermediates of mRNA that may not have been reverse-transcribed into cDNA. Nucleic acid having protein coding sequence may be obtained by surreening selected cDNA or genomic

Selection and Transformation of Host Cells

principles, protocols, and practical techniques for maximizing the productivity of cell cultures can be found in Mammalian Cell Biotechnology; a Practical Approach, M. Butler, ed. (IRL Press, 1991) and Sambrook et al. temperature, pH and the like, can be selected by the skilled artisan without undue experimentation. In general, production and cultured in conventional nutrient media modified as appropriate for inducing promoters, selecting transformants, or amplifying the genes encoding the desired sequences. The culture conditions, such as media, Host cells are transfected or transformed with expression or cloning vectors described herein for PRC

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20 2 5 also be used. For various techniques for transforming mammalian cells, see Keown et al., Methods in 52:456-457 (1978) can be employed. General aspects of mammalian cell bost system transfections have been used, transformation is performed using standard techniques appropriate to such cells. The calcium treatment electroporation, bacterial protoplast fusion with intact cells, or polycations, c.g., polybrene, polyomithine, may (1979). However, other methods for introducing DNA into cells, such as by nuclear microinjection, method of Van Solingen et al., <u>J. Barg., 130</u>:946 (1977) and Hsiao et al., <u>Proc. Natl. Acad. Sci. (USA), 76</u>:3829 prokaryotes. Infection with Agrobacterium tumefacters is used for transformation of certain plant cells, as Enzymology, 185:527-537 (1990) and Mansour et al., Nanuc, 336:348-352 (1988). described in U.S. Patent No. 4,399,216. Transformations into yeast are typically carried out according to the without such cell walls, the calcium phosphate precipitation method of Graham and van der Eb. Virology, described by Shaw et al., Gene, 23:315 (1983) and WO 89/05859 published 29 June 1989. For mammalian cells employing calcium chloride, as described in Sambrook et al., supra, or electroporation is generally used for skilled artisan, for example, CaCl₁, CaPO₄, liposome-mediated and electroporation. Depending on the host cell Methods of eukaryotic cell transfection and prokaryotic cell transformation are known to the ordinarily

25 ton4 : E. coli W3110 strain 9E4, which has the complete genotype ton4 ptr3; E. coli W3110 strain 27C7 W3110 strain 37D6, which has the complete genotype tonA ptr3 phaA E15 (argF-lac)169 degP ompT rbs7 Pseudomonas such as P. aeruginosa, and Streptomyces. These examples are illustrative rather than limiting publicly available, such as E. coli K12 strain MM294 (ATCC 31,446); E. coli X1776 (ATCC 31,537); E. coli (ATCC 55,244), which has the complete genotype tond ptr3 phod E15 (argF-lac)169 degP ompT kart'; E. coli to the host, with examples of such hosts including E. coli W3110 strain 1A2, which has the complete genotype example, strain W3110 may be modified to effect a genetic mutation in the genes encoding proteins endogenous DNA product fermentations. Preferably, the host cell secretes minimal amounts of proteolytic enzymes. For Strain W3110 is one particularly preferred bost or parent host because it is a common host strain for recombinant e.g., Salmonella typhimurium, Serratia, e.g., Serratia marcescans, and Shigella, as well as Bocilli such as B or Gram-positive organisms, for example, Enterobacteriaceae such as E. coli. Various E. coli strains are or higher eukaryote cells. Suitable prokaryotes include but are not limited to eubacteria, such as Gram-negative subilits and B. licheniformis (e.g., B. licheniformis 41P disclosed in DD 266,710 published 12 April 1989), strain W3110 (ATCC 27,325) and KS 772 (ATCC 53,635). Other suitable prokaryotic host cells include Enterobacterincene such as Escherichia, e.g., E. coli, Enterobacter, Erwinia, Klebsielia, Proteus, Salmonella Suitable thost cells for cloning or expressing the DNA in the vectors herein include prokaryote, yeast,

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7 August 1990. Alternatively, in virro methods of cloning, e.g., PCR or other nucleic acid polymerase reactions mutation: and an E. coli strain having mutant periplasmic protease disclosed in U.S. Patent No. 4,946,783 issued ilvG kan'; E. coli W3110 strain 40B4, which is strain 37D6 with a non-kanamycin resistant degP deletion

or expression hosts for PRO-encoding vectors. Saccharomyces cerevisiae is a commonly used lower eubaryotic EP 139,383 published 2 May 1985); Kluyveromyces hasis (U.S. Patent No. 4,943,529; Fleer et al. host microorganism. Others include Schizosaccharomyces pombe (Beach and Nurse, Nature, 290: 140 [1981] <u>l. Bacteriol.</u>, 737 (1983)), K. fragilis (ATCC 12,424), K. bulgaricus (ATCC 16,045), K. wickeramii (ATCC <u>Bio/Technology</u>, 9:968-975 (1991)) such as, e.g., K. lactis (MW98-8C, CBS683, CBS4574; Louvencourt et al., In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are suitable cloning

5 24,178), K. walii (ATCC 56,500), K. drosophilarum (ATCC 36,906; Van den Berg et al., Bio/Technology Steekrishna et al., J. Basic Microbiol., 28:265-278 [1988]); Candida: Trichoderma reesia (EP 244,234); Schwamiomyces occidenalis (EP 394.538 published 31 October 1990); and filamentous fungi such as. e.g., 8:135 (1990)), K. thermotolerans, and K. marxianus; yarrowia (EP 402,226); Pichia pastoris (EP 183,070) Neurospora crassa (Case et al., Proc. Natl. Acad. Sci. USA, 76:5259-5263 [1979]); Schwanniomyces such as

5 Neurospora, Penicillium, Totypocladium (WO 91/00357 published 10 January 1991), and Aspergillus hosts such to, yeast capable of growth on methanol selected from the genera consisting of Hansenula, Candida, Kloeckera, 26:205-221 [1983]; Yelton et al., Proc. Natl. Acad. Sci., USA, 81: 1470-1474 [1984]) and A. alger (Kelly and as A. nidulars (Ballance et al., Biochem, Biophys, Res. Commun., 112:284-289 [1983]; Tilburn et al., Gene. Hymes, EMBOL, 4:475-479 [1985]). Methylotropic yeasts are suitable herein and include, but are not limited

8 of years may be found in C. Anthony, The Biochemistry of Methylogophs, 269 (1982). Pichia, Sacchuromyces, Torulopsis, and Rhodosonula. A list of specific spectes that are exemplary of this class

30 23 060562, ATCC CCL51). The selection of the appropriate bost cell is deemed to be within the skill in the art cells (W138, ATCC CCL 75); human liver cells (Hep G2, IIB 8065); and mouse mammary tumor (MMT More specific examples include monkey kidney CV1 time transformed by SV40 (COS-7, ATCC CRL 1651); Sci. USA, 77:4216 (1980)); mouse sectoli cells (TM4, Mather, Biol. Reprod., 23:243-251 (1980)); human lung human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture. Graham et al., I_ Examples of invertebrate cells include insect cells such as Drosophila S2 and Spodoptera S69, as well as plant Gen Virol., 36:59 (1977)); Chinese hamster ovary cells/-DHFR (CHO, Urlaub and Chasin, Proc. Natl. Acad. cells. Examples of useful mammalian host cell lines include Chinese hamster ovary (CHO) and COS cells Suitable host cells for the expression of glycosylated PRO are derived from multicellular organisms

Selection and Use of a Replicable Vector

35 may, for example, be in the form of a plaxmid, cosmid, viral particle, or phage. The appropriate nucleic acid for cloning (amplification of the DNA) or for expression. Various vectors are publicly available. The vector appropriate restriction endonuclease site(s) using techniques known in the arr. Vector components generally sequence may be inserted into the vector by a variety of procedures. In general, DNA is inserted into an The nucleic acid (e.g., cDNA or genomic DNA) encoding PRO may be inserted into a replicable vector

include, but are not limited to, one or more of a signal sequence, an origin of replication, one or more market vectors containing one or more of these components employs standard ligation techniques which are known to genes, an enhancer element, a promoter, and a transcription termination sequence. Construction of suitable

Ş heterologous polypeptide, which may be a signal sequence or other polypeptide having a specific cleavage site penicillinase, lpp, or hear-stable enterotoxin Il leaders. For yeast secretion the signal sequence may be, e.g., may be a prokaryotic signal sequence selected, for example, from the group of the alkaline phosphatase, the vector, or it may be a part of the PRO-encoding DNA that is inserted into the vector. The signal sequence at the N-terminus of the manure protein or polypeptide. In general, the signal sequence may be a component of The PRO may be produced recombinantly not only directly, but also as a fusion polypeptide with

5 5 the yeast invertase leader, alpha factor leader (including Saccharomyces and Klayveromyces a-factor leaders secretory leaders. protein, such as signal sequences from secreted polypeptides of the same or related species, as well as vital 1990. In mammalian cell expression, mammalian signal sequences may be used to direct secretion of the the latter described in U.S. Patent No. 5,010,182), or acid phosphatase leader, the C. albicans glucoamylase leader (EP 362,179 published 4 April 1990), or the signal described in WO 90/13646 published 15 November

cloning vectors in mammalian cells. origin is suitable for yeast, and various viral origins (SV40, polyoma, adenovirus, VSV or BPV) are useful for The origin of replication from the plasmid pBR322 is suitable for most Gram-negative bacteria, the 2μ plasmid in one or more selected host cells. Such sequences are well known for a variety of bacteria, yeast, and viruses Both expression and cloning vectors contain a nucleic acid sequence that enables the vector to replicate

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not available from complex media, e.g., the gene encoding D-alanine racemase for Bacilli. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxins, e.g., ampicillin neomycin, methotrexate, or tetracycline, (b) complement auxotrophic deficiencies, or (c) supply critical nurients Expression and closing vectors will typically contain a selection gene, also termed a selectable marker

8 ઇ ATCC No. 44076 or PEP4-1 [Jones, Genetics, 85:12 (1977)]. provides a selection marker for a mutaut strain of yeast lacking the ability to grow in tryptophan, for example, 282:39 (1979); Kingaman et al., Gene, 7:141 (1979); Techemper et al., Gene, 10:157 (1980)]. The trp1 gene prepared and propagated as described by Urlaub et al., Proc. Natl. Acad. Sci. USA, 77:4216 (1980). A suitable appropriate host cell when wild-type DHFR is employed is the CHO cell line deficient in DHFR activity of cells competent to take up the PRO-encoding nucleic acid, such as DHFR or thymidine kinase. An selection gene for use in yeast is the up1 gene present in the yeast plasmid YRp7 [Stinchcomb et al., Nature, An example of suitable selectable markers for mammalian cells are those that enable the identification

딿 known. Promoters suitable for use with prokaryotic hosts include the β -lactamase and lactose promoter systems [Chang et al., Nature, 275:615 (1978); Greeddel et al., Nature, 281:544 (1979)], alkaline phosphause, a acid sequence to direct mRNA symbosis. Promoters recognized by a variety of potential host cells are well tryptophan (trp) promoter system (Goeddel, Nucleic Acids Res., 8:4057 (1980); EP 36,776], and hybrid Expression and cloning vectors usually contain a promoter operably linked to the PRO-encoding nucleic

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for use in bacterial systems also will contain a Shine-Dalgarno (S.D.) sequence operably linked to the DNA promoters such as the tac promoter [deBoer et al., Proc. Natl. Acad. Sci. USA, 80:21-25 (1983)]. Promoten

Ŋ et al., J. Adv. Enzyme Reg., 7:149 (1968); Holland, Biochemistry, 17:4900 (1978)], such as enolase phosphoglycerate kinase [Hitzeman et al., <u>L. Bjol., Chem.,</u> 255:2073 (1980)] or other glycolytic enzymes [Hess 6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphateisomerase, phosphoglucose glyceraldehyde-3-phosphate dehydrogemase, hexokinase, pyruvatedecarboxylase, phosphofructokinase, glucoseisomerase, and glucokinase. Examples of suitable promoting sequences for use with yeast hosts include the promoters for 3-

ö controlled by growth conditions, are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization. Suitable vectors and phosphatase, degradative enzymes associated with nitrogen metabolism, metallothionein, glyceraldehyde-3promoters for use in yeast expression are further described in EP 73,657 Other yeast promoters, which are inducible promoters having the additional advantage of transcription

2 obtained from the genomes of viruses such as polyuma virus, fow/pox virus (UK 2,211,504 published 5 July compatible with the host cell systems. retrovirus, hepatitis-B virus and Simian Virus 40 (SV40), from heterologous mammalian promoters, e.g., the actin promoter or an immunoglobulin promoter, and from heat-shock promoters, provided such promoters are 1989), adenovirus (such as Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus, a PRO transcription from vectors in mammalian host cells is controlled, for example, by promoters

25 20 origin (bp 100-270), the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the bp, that act on a promoter to increase its transcription. Many enhancer sequences are now known from enhancer sequence into the vector. Enhancers are cis-acting elements of DNA, usually about from 10 to 300 enhancer from a enkaryotic cell virus. Examples include the SV40 enhancer on the late side of the replication mammalian genes (globin, elastase, nibumin, a-fetoprotein, and insulin). Typically, however, one will use an Transcription of a DNA encoding the PRO by higher eukaryotes may be increased by inserting an

cells from other multicellular organisms) will also contain sequences necessary for the termination of 3' to the PRO coding sequence, but is preferably located at a site 5' from the promoter. Expression vectors used in eukaryotic host cells (yeast, fungi, insect, plant, animal, human, or nucleated

replication origin, and adenovirus enhancers. The enhancer may be spliced into the vector at a position 5' or

30 transcription and for stabilizing the mRNA. Such sequences are commonly available from the 5' and occasionally 3', untranslated regions of enteryotic or viral DNAs or cDNAs. These regions contain nucleotide segments transcribed as polyadenylated fragments in the untranslated portion of the mRNA encoding PRO.

35 recombinant vertebrate cell culture are described in Gething et al., Nature, 293:620-625 (1981); Mantei et al. Still other methods, vectors, and host cells suitable for adaptation to the synthesis of PRO in

Nature, 281:40-46 (1979); EP 117,060; and EP 117,058

Detecting Gene Amplification/Expression

that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes to the duplex can be detected. duplex is bound to a surface, so that upon the formation of duplex on the surface, the presence of antibody bound or DNA-protein duplexes. The antibodies in turn may be labeled and the assay may be carried out where the appropriately labeled probe, based on the sequences provided herein. Alternatively, antibodies may be employed Acad. Sci. USA, 77:5201-5205 (1980)], dot blotting (DNA analysis), or in sim hybridization, using an conventional Southern blotting, Northern blotting to quantitate the transcription of mRNA [Thomas, Proc. Natl. Gene amplification and/or expression may be measured in a sample directly, for example, by

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immunohistochemical staining of cells or tissue sections and assay of cell culture or body fluids, to quantitate the DNA sequences provided herein or against exogenous sequence fused to PRO DNA and encoding a specific antibodies may be prepared against a native sequence PRO polypeptide or against a symbetic peptide based on sample fluids may be either motocolonal or polyclonal, and may be prepared in any mammal. Conveniently, the directly the expression of gene product. Antibodies useful for immunohistochemical staining and/or assay of Gene expression, alternatively, may be measured by immunological methods, such as

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Purification of Polypeptide

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8 cleavage. Cella employed in expression of PRO can be disrupted by various physical or chemical means, such it can be released from the membrane using a suitable detergent solution (e.g. Triton-X 100) or by enzymatic as freeze-thaw cycling, sonication, mechanical disruption, or cell lysing agents. Forms of PRO may be recovered from outhine medium or from host cell lysates. If membrane-bound

25 DEAE; chromatofocusing; SDS-PAGE; ammonium sulfate precipitation; gel filtration using, for example, methods are known in the art and described for example in Deutscher, Methods in Empymology, 182 (1990); to bind epitope-tagged forms of the PRO. Various methods of protein purification may be employed and such Sephadex G-75; protein A Sepharose columns to remove contaminants such as IgG; and metal chelating columns Scopes, Protein Purification: Principles and Practice, Springer-Verlag, New York (1982). The purification procedures are exemplary of suitable purification procedures: by fractionation on an ion-exchange column; thanol precipitation; reverse phase HPLC; chromatography on silica or on a cation-exchange resin such as It may be desired to purify PRO from recombinant cell proteins or polypeptides. The following

30 step(s) selected will depend, for example, on the nature of the production process used and the particular PRO

E. Uses for PRO

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molecular biology, including uses as hybridization probes, in chromosome and gene mapping and in the generation of anti-sense RNA and DNA. PRO nucleic acid will also be useful for the preparation of PRO Nucleotide sequences (or their complement) encoding PRO have various applications in the art of

polypeptities by the recombinant techniques described herein.

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5 probe via avidin/hiotin coupling systems. Labeled probes having a sequence complementary to that of the PRO nucleotide sequence wherein those regions may be determined without undue experimentation or from genomic to synthesize a selected probe of about 40 bases. Hybridization probes may be labeled by a variety of labels a screening method will comprise isolating the coding region of the PRO gene using the known DNA sequence further detail in the Examples below. determine which members of such libraries the probe hybridizes 10. Hybridization techniques are described in including radionucleotides such as 32P or 33S, or enzymatic labels such as alkaline phosphatase coupled to the sequences including promoters, enhancer elements and introns of native sequence PRO. By way of example bases. The hybridization probes may be derived from at least partially novel regions of the full length nariw to the native PRO sequence disclosed herein. Optionally, the length of the probes will be about 20 to about 50 for a cDNA library to isolate the full-length PRO cDNA or to isolate still other cDNAs (for instance, those gene of the present invention can be used to screen libraries of human cDNA, genomic DNA or mRNA to encoding naturally-occurring variants of PRO or PRO from other species) which have a desired sequence identity The full-length native sequence PRO gene, or portions thereof, may be used as hybridization probe

the methods disclosed herein. Any EST sequences disclosed in the present application may similarly be employed as probes, using

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20 Cohen (Cancer Res. 48:2659, 1988) and van der Krol et al. (BioTechniques 6:958, 1988). oligonucleoride, based upon a cDNA sequence encoding a given protein is described in, for example, Stein and nucleotides, preferably from about 14 to 30 nucleotides. The ability to derive an antisense or a sense comprise a fragment of the coding region of PRO DNA. Such a fragment generally comprises at least about 14 or PRO DNA (antisense) sequences. Antisense or sense oligomucleotides, according to the present invention, a singe-stranded nucleic acid sequence (either RNA or DNA) capable of binding to target PRO mRNA (sense) Other useful fragments of the PRO nucleic acids include antisense or sense oligonucleotides comprising

8 25 resisting enzymatic degradation) but retain sequence specificity to be able to bind to target nucleotide sequences. The antisense oligonucleotides thus may be used to block expression of PRO proteins. Antisense or sense enhanced degradation of the duplexes, premature termination of transcription or translation, or by other means. of duplexes that block transcription or translation of the target sequence by one of several means, including cudogenous nucleases. Such oligonucleotides with resistant sugar linkages are stable in vivo (i.e., capable of sugar linkages, such as those described in WO 91/06629) and wherein such sugar linkages are resistant to oligonucleotides further comprise oligonucleotides having modified sugar-phosphodiester backbones (or other Binding of antisense or sense oligonucleotides to target nucleic acid sequences results in the formation

发 nucleotide sequence. antisense oligonucleorides to modify binding specificities of the antisense or sense oligonucleoride for the target intercalating agents, such as ellipticine, and alkylating agents or metal complexes may be attached to sense or covalently linked to organic mototics, such as those described in WO 90/10048, and other moteties that increases affinity of the oligonucleotide for a target nucleic acid sequence, such as poly-(L-lysine). Further still, Other examples of sense or antisense oligonucleorides include those oligonucleorides which are

Antiseuse or sense oligonucleotides may be introduced into a cell containing the target nucleic acid

sequence by any gene transfer method, including, for example, CaPO_x-mediated DNA transfection, electroporation, or by using gene transfer vectors such as Epstein-Barr virus. In a preferred procedure, an autisense or sense oligonucleotide is inserted into a suitable retroviral vector. A cell containing the target nucleic acid sequence is contacted with the recombinant retroviral vector, either in vivo or ex vivo. Suitable retroviral vectors include, but are not limited to, those derived from the murine retrovirus M-MuLV, N2 (a retrovirus vectors include, but are not limited to, those derived from the murine retrovirus M-MuLV, N2 (a retrovirus derived from M-MuLV), or the double copy vectors designated DCT5A, DCT5B and DCT5C (see WO 90/13641).

Sense or antisense ollgonucleotides also may be introduced into a cell containing the target nucleotide sequence by formation of a conjugate with a ligand binding molecule, as described in WO 91/04753. Suitable ligand binding molecules include, but are not limited to, cell surface receptors, growth factors, other cytokines, or other ligands that bind to cell surface receptors. Preferably, conjugation of the ligand binding molecule does not substantially interfere with the ability of the ligand binding molecule to bind to its corresponding molecule or receptors, or block entry of the sense or antisense oligonucleotide or its conjugated version into the cell.

Alternatively, a sense or an amisense oligonucleotide may be introduced into a cell containing the target nucleic acid sequence by formation of an oligonucleotide-lipid complex, as described in WO 90/10448. The sense or antisease oligonucleotide-lipid complex is preferably dissociated within the cell by an endogenous lipase.

The probes may also be employed in PCR techniques to generate a pool of sequences for identification of closely related PRO coding sequences.

Neclocide sequences encoding a PRO can also be used to construct hybridization probes for mapping the gene which encodes that PRO and for the genetic analysis of individuals with genetic disorders. The 20 auctooride sequences provided herein may be mapped to a chromosome and specific regions of a chromosome using known techniques, such as in situ hybridization, linkage analysis against known chromosomal markers, and hybridization screening with libraries.

When the coding sequences for PRO encode a protein which binds to another protein (example, where the PRO is a receptor), the PRO can be used in assays to identify the other proteins or molecules involved in the PRO can be used in assays to identify the other proteins or molecules involved in the Proteins involved in such bhiding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction. Also, the receptor PRO can be used to isolate correlative ligand(s). Screening assays can be designed to find lead compounds that mimic the biological activity of a native PRO or a receptor for PRO. Such actrening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates. Small molecules contemplated include synthetic organic or inorganic compounds. The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays and cell based assays, which are well characterized in the art.

Nucleic acids which encode PRO or its modified forms can also be used to generate either transgenic animals or 'knock out' animals which, in turn, are useful in the development and screening of therapeutically useful reagents. A transgenic animal (e.g., a mouse or rat) is an animal having cells that contain a transgene, which transgene was introduced into the animal or an ancestor of the animal at a prematal, e.g., an embryonic

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stage. A transgene is a DNA which is integrated into the genome of a cell from which a transgenic animal develops. In one embodiment, cDNA encoding PRO can be used to clone genomic DNA encoding PRO in accordance with established techniques and the genomic sequences used to generate transgenic animals that contain cells which express DNA encoding PRO. Methods for generating transgenic animals, particularly animals such as mice or rats, have become convemional in the art and are described, for example, in U.S. Patent S Nos. 4.736,866 and 4.870,009. Typically, particular cells would be targeted for PRO transgenic incorporation with tissue-specific enhancers. Transgenic animals that include a copy of a transgene encoding PRO introduced into the germ line of the animal at an embryonic stage can be used to examine the effect of increased expression of DNA encoding PRO. Such animals can be used as tester animals for reagents thought to confer protection from, for example, pathological conditions associated with its overexpression. In accordance with this facet of the invention, an animal is trusted with the reagent and a reduced incidence of the pathological condition, compared to untreased animals bearing the transgene, would indicate a potential therepeutic increvention for the pathological condition.

30 2 8 endogenous gene encoding PRO and altered genomic DNA encoding PRO introduced into an embryonic stem the PRO polypeptide. against certain pathological conditions and for their development of pathological conditions due to absence of a "knock out" animal. Progeny harboring the homologously recombined DNA in their germ cells can be then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term to create Cells: A Practical Approach, E. J. Robertson, ed. (IRL, Oxford, 1987), pp. 113-152]. A chimeric embryo can c.g., Li et al., Cell, 69:915 (1992)]. The selected cells are then injected into a blastocyst of an animal (e.g., cells in which the introduced DNA has homologously recombined with the endogenous DNA are selected [see in the vector [see e.g., Thomas and Capocchi, Cell, 51:503 (1987) for a description of homologous cell of the animal. For example, cDNA encoding PRO can be used to clone genomic DNA encoding PRO in a mouse or (at) to form aggregation chimeras (see e.g., Bradley, in Terarocarcinomas and Embryonic Stem recombination vectors). The vector is introduced into an embryonic stem cell line (e.g., by electroporation) and accordance with established techniques. A portion of the genomic DNA encoding PRO can be deleted or identified by standard techniques and used to breed animals in which all cells of the animal contain the which has a defective or altered gene encoding PRO as a result of homologous recombination between the replaced with another gene, such as a gene encoding a selectable marker which can be used to monitor tomologously recombined DNA. Knockout animals can be characterized for instance, for their ability to defend integration. Typically, several kilobases of unaltered flanking DNA (both at the 5' and 3' ends) are included Alternatively, non-human homologues of PRO can be used to construct a PRO "knock out" arimal

Nucleic acid encoding the PRO polypeptides may also be used in gene therapy. In gene therapy applications, genes are immoduted into cells in order to achieve in vivo synthesis of a therapeutically effective genetic product, for example for replacement of a defective gene. "Gene therapy" includes both conventional gene therapy where a laxting effect is achieved by a single treatment, and the administration of gene therapeutic agents, which involves the one time or repeated administration of a therapeutically effective DNA or mRNA. Antisense RNAs and DNAs can be used as therapeutic agents for blocking the expression of certain genes.

vivo. It has already been shown that short antisense oligomucleotides can be imported into cells where they act as inhibitors, despite their tow intracellular concentrations caused by their restricted uptake by the cell membrane. (Zamecruk et al., <u>Proc. Natl. Acad. Sci. USA</u> 83:4143-4146 [1986]). The oligomucleotides can be modified to enhance their uptake, e.g. by substituting their negatively charged phosphodiester groups by uncharged groups.

- 10 uptake, e.g. capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which (typically retroviral) vectors and viral cost procein-tiposome mediated transfection (Dzau et al., Trends in marking and gene therapy protocols see Anderson et al., Science 256, 808-813 (1992). 4429-4432 (1987); and Wagner et al., Proc. Natl. Acad. Sci. USA 87, 3410-3414 (1990). For review of gene The technique of receptor-mediated endocytosis is described, for example, by Wu et al., L.Biol. Chem. 262 to a cell surface membrane protein associated with endocytosis may be used for targeting and/or to facilitate target cell, a ligand for a receptor on the target cell, etc. Where liposomes are employed, proteins which bind an agent that targets the target cells, such as an antibody specific for a cell surface membrane protein or the undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half-life precipitation method, etc. The currently preferred in vivo gene transfer techniques include transfection with viral include the use of liposomes, electroporation, microinjection, cell fusion, DEAE-dextran, the calcium phosphate the cells of the intended host. Techniques suitable for the transfer of nucleic acid into mammalian cells in virro techniques vary depending upon whether the nucleic acid is transferred into cultured cells in vitro, or in vivo in Biotechnology, 11, 205-210 (1993)). In some situations it is desirable to provide the nucleic acid source with There are a variety of techniques available for introducing nucleic acids into viable cells. The
- 20 The PRO polypepides described herein may also be employed as molecular weight markers for protein electrophoresis purposes and the isolated nucleic acid sequences may be used for recombinantly expressing those markers.

The nucleic acid molecules encoding the PRO polypeptides or fragments thereof described herein are useful for chromosome identification. In this regard, there exists an ongoing need to identify new chromosome markers, since relatively few chromosome marking reagents, based upon actual sequence data are presently available. Each PRO nucleic acid molecule of the present invention can be used as a chromosome marker.

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The PRO polypeptides and nucleiz acid molecules of the present invention may also be used for tissue typing, wherein the PRO polypeptides of the present invention may be differentially expressed in one tissue as compared to another. PRO mucleic acid molecules will find use for generating probes for PCR, Northern analysis, Southern analysis and Western analysis.

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The PRO polypeptides described herein may also be employed as therapeutic agents. The PRO polypeptides of the present invention can be formulated according to known methods to prepare pharmaceutically useful compositions, whereby the PRO product hereof is combined in admixture with a pharmaceutically acceptable carrier vehicle. Therapeutic formulations are prepared for storage by mixing the active ingredient having the desired degree of purity with optional physiologically acceptable carriers, excipients or stabilizers (Remineroutical Sciences 16th edition, Onol, A. Ed. (1980)), in the form of hyophilized formulations or aqueous solutions. Acceptable carriers, excipients or stabilizers are monoxic to recipients at the

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dvzages and concentrations employed, and include buffers such as phosphate, citrate and other organic acids; anioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin or immunoglobulins; hydrophilic polymets such as polyvinylpytrollidone, amino acids such as glycine, glutamine, asparagine, arginine or lytine; monosaccharides, disaccharides and other carbothydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; sall-forming counterions such as acidium; and/or nonionic surfactants such as TWEENT, PLURONICSTM or PEG.

The formulations to be used for *in vivo* administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes, prior to or following lyophilization and reconstitution.

Therapeutic compositions herein generally are placed into a container having a sterile access port, for 10 example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

The route of administration is in accord with known methods, e.g. injection or infusion by intravenous, intrapertional, intractebral, intramuscular, intraocular, intraarterial or intralesional routes, topical administration, or by sustained release systems.

Datages and desired drug concentrations of pharmacountral compositions of the present invention may depending on the particular use envisioned. The determination of the appropriate dosage or route of administration is well within the skill of an ordinary physician. Animal experiments provide reliable guidance for the determination of effective doses for human therapy. Interspecies scaling of effective doses can be performed following the principles laid down by Mordenti, J. and Chappell, W. 'The use of interspecies scaling in toxicokinetics' In Toxicokinetics and New Drug Development, Yacobi et al., Eds., Pergamon Press, New 20 York 1989, pp. 42-96.

When in vivo administration of a PRO polypeptide or agonist or antagonist thereof is employed, normal dosage amounts may vary from about 10 ng/kg to up to 100 mg/kg of mammal body weight or more per day, preferably about 1 µg/kg/day to 10 mg/kg/day, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature; see, for example, U.S. Pat. Nos. 2.5 4,657,769; 5,206,344; or 5,225,212. It is atticipated that different formulations will be effective for different treatment compounds and different disorders, that administration targeting one organ or tissue, for example, may necessitate delivery in a mamoer different from that to another organ or tissue.

Where sustained-release administration of a PRO polypeptide is desired in a formulation with release characteristics suitable for the treatment of any disease or disorder requiring administration of the PRO polypeptide, microencapsulation of the PRO polypeptide is contemplated. Microencapsulation of recombinant proteins for sustained release has been successfully performed with human growth hormone (rhGH), interferon. (rhHPN-), interleukin-2, and MN 1gp120. Johnson et al., Nst. Med., 2:795-799 (1996); Yasuda, Biomed Thet., 27:1221-1223 (1993); Hora et al., BioTechnology, 8:735-758 (1990); Cleband, "Design and Production of Single Immunization Vaccines Using Polylactide Polyglycolide Microsphere Systems," in Vaccine Design.

35 The Submit and Adjuvant Addrovatch, Powell and Newman, eds. (Plenum Press: New York, 1995), pp. 439-462; WO 97/03692, WO 96/0702, WO 96/07399; and U.S. Pat. No. 5,654,010.

The sustained-release formulations of these proteins were developed using poly-lactic-coglycolic acid

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R. Langer (Eds.), Biodegradable Polymers as Drug Delivery Systems (Marcel Dekker: New York, 1990), pp. composition. Lewis, "Controlled release of bloactive agents from lactide/glycolide polymer," in: M. Chasin and degradability of this polymer can be adjusted from months to years depending on its molecular weight and (PLGA) polymer due to its biocompatibility and wide range of biodegradable properties. The degradation products of PLGA, lactic and glycolic acids, can be cleared quickly within the human body. Moreover, the

with other cellular proteins. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates. encoded by the genes identified herein, or otherwise interfere with the interaction of the encoded polypeptides antagonist drug candidates are designed to identify compounds that bind or complex with the PRO polypeptides polypeptide (agonists) or prevent the effect of the PRO polypeptide (antagonists). Screening assays for This invention encompasses methods of screening compounds to identify those that mimic the PRO

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biochemical screening assays, inununoassays, and cell-based assays, which are well characterized in the art. The assays can be performed in a variety of formats, including protein-protein binding assays

5 polypeptide encoded by a nucleic acid identified herein under conditions and for a time sufficient to allow these two components to interact. All assays for antagonists are common in that they call for contacting the drug candidate with a PRO

25 20 non-reacted components are removed, e.g., by washing, and complexes anchored on the solid surface are attachments. Non-covalent attachment generally is accomplished by coating the solid surface with a solution of detected. When the originally non-immobilized component carries a detectable label, the detection of label by adding the non-immohilized component, which may be labeled by a detectable label, to the immobilized for the PRO polypeptide to be immobilized can be used to anchor it to a solid surface. The assay is performed the PRO polypeptide and drying. Alternatively, an immobilized antibody, e.g., a monocional antibody, specific specifically binding the immobilized complex. component does not carry a label, complexing can be detected, for example, by using a labeled amibody immobilized on the surface indicates that complexing occurred. Where the originally non-immobilized component, e.g., the coated surface containing the anchored component. When the reaction is complete, the drug candidate is immobilized on a solid phase, e.g., on a microtiter plate, by covalent or non-covalent reaction mixture. In a particular embodiment, the PRO polypeptide encoded by the gene identified herein or tho In binding assays, the interaction is binding and the complex formed can be isolated or detected in the

Š 30 (Fields and Song, Nature (London), 340:245-246 (1989); Chien et al., Proc. Natl. Acad. Sci. USA, 88:9578 a gene identified herein, its interaction with that polypeptide can be assayed by methods well known for detecting transcriptional activators, such as yeast GALA, consist of two physically discrete modular domains, one acting 9582 (1991)) as disclosed by Chevray and Nathans, Proc. Natl. Acad. Sci. USA, 89: 5789-5793 (1991). Many protein interactions can be monitored by using a yeast-based genetic system described by Fields and co-workers immunoprecipitation, and co-purification through gradients or chromatographic columns. In addition, protein protein-protein interactions. Such assays include traditional approaches, such as, c.g., cross-linking, co-If the candidate compound interacts with but does not bind to a particular PRO polypeptide encoded by

5 depends on reconstitution of GALA activity via protein-protein interaction. Colonies comaining interacting these interactions. hybrid technique is commercially available from Clontech. This system can also be extended to map protein (MATCHMAKERTM) for identifying protein-protein interactions between two specific proteins using the twothe DNA-binding domain of GALA, and another, in which candidate activating proteins are fused to the domains involved in specific protein interactions as well as to pinpoint amino acid residues that are crucial for polypeptides are detected with a chromogenic substrate for \$\textit{b-galactosidase}. A complete kit activation domain. The expression of a GAL1-lac2 reporter gene under control of a GAL4-activated promoter takes advantage of this property, and employs two hybrid proteins, one in which the target protein is fused to expression system described in the foregoing publications (generally referred to as the "two-hybrid system") as the DNA-binding domain, the other one functioning as the transcription-activation domain. The year

inhibit binding, the reaction is run in the absence and in the presence of the test compound. In addition, a and its reaction partner. between the test compound and the intra- or extracellular component present in the mixture is monitored as placebo may be added to a third reaction mixture, to serve as positive control. The binding (complex formation) and other intra- or extracellular components can be tested as follows: usually a reaction mixture is prepared containing the test compound indicates that the test compound interferes with the interaction of the test compound described hereinabove. The formation of a complex in the control reaction(s) but not in the reaction mixture allowing for the interaction and binding of the two products. To test the ability of a candidate compound to containing the product of the gene and the intra- or extracellular component under conditions and for a time Compounds that interfere with the interaction of a gene encoding a PRO polypeptide identified herein

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3 30 ટ incubation, the slides are subjected to autoradiographic analysis. Positive pools are identified and sub-pools are cells or other cells that are not responsive to the PRO polypeptide. Transfected cells that are grown on glass the PRO polypeptide and a cDNA library created from this RNA is divided into pools and used to transfest COS Preferably, expression cloning is employed wherein polyadenylated RNA is prepared from a cell responsive to PRO polypeptide receptors or recombinant receptors under appropriate conditions for a competitive inhibition prepared and re-transfected using an interactive sub-pooling and re-screening process, eventually yielding a molecules bound to the receptor can be used to determine the effectiveness of the potential antagonist. The gene assay. The PRO polypeptide can be labeled, such as by radioactivity, such that the number of PRO polypeptide of the PRO polypeptide indicates that the compound is an antagonist to the PRO polypeptide. Alternatively, slides are exposed to labeled PRO polypeptide. The PRO polypeptide can be labeled by a variety of means ligand panning and FACS sorting. Collgan et al., Current Protocols in Immun., 1(2): Chapter 5 (1991) single clone that encodes the putative receptor. including iodination or inclusion of a recognition site for a site-specific protein kinase. Following fixation and encoding the receptor can be identified by numerous methods known to those of skill in the art, for example, antagonists may be detected by combining the PRO polypeptide and a potential antagonist with membrane-bound screened for a particular activity and the ability of the compound to inhibit the activity of interest in the presence To assay for antagonists, the PRO polypeptide may be added to a cell along with the compound to be

As an alternative approach for receptor identification, labeled PRO polypeptide can be photosiffunitylinked with cell membrane or extract preparations that express the receptor molecule. Cross-linked material is
resolved by PAGE and exposed to X-ray film. The labeled complex containing the receptor can be excised,
resolved into peptide fragments, and subjected to protein micro-sequencing. The amino acid sequence obtained
from micro-sequencing would be used to design a set of degenerate oligonucleotide probes to screen a cDNA
library to identify the gene encoding the putative receptor.

In another assay for an agonists, mammalian cells or a membrane preparation expressing the receptor would be incubated with labeled PRO polypeptide in the presence of the candidate compound. The ability of the compound to enhance or block this interaction could then be measured.

More specific examples of potential antagonists include an oligonucleotide that binds to the fusions of immunoglobulin with PRO polypepide, and, in particular, amibodies including, without limitation, poly- and monoclonal antibodies and antibody fragments, single-chain antibodies, anti-idioxypic antibodies, and chimeric or humanized versions of such antibodies or fragments, as well as human antibodies and antibody fragments. Alternatively, a potential antagonist may be a closely related protein, for example, a mutated form of the PRO polypeptide that recognizes the receptor but imparts no effect, thereby competitively inhibiting the action of the PRO polypeptide.

೪ ĸ 8 polypeptide. When antisense DNA is used, oligodeoxyribonucleotides derived from the translation-initiation site. preventing transcription and the production of the PRO polypeptide. The antisense RNA oligonucleotide based on binding of a polynucleotide to DNA or RNA. For example, the 5' coding portion of the polynucleotide e.g., between about -10 and +10 positions of the target gene nucleotide sequence, are preferred. to cells such that the antisense RNA or DNA may be expressed in vivo to inhibit production of the PRO (antisense - Okano, Neurochem., 56:56) (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene tybridizes to the mRNA in vivo and blocks translation of the mRNA molecule into the PRO polypeptide 6:3073 (1979); Cooney et al., Science, 241: 456 (1988); Dervan et al., Science, 251:1360 (1991)), thereby complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res. oligonucleotide of from about 10 to 40 base pairs in length. A DNA oligonucleotide is designed to be sequence, which encodes the mature PRO polypeptides herein, is used to design an antisense RNA mRNA by hybridizing to targeted mRNA and preventing protein translation. Antisense technology can be used to control gene expression through triple-helix formation or antisense DNA or RNA, both of which methods are antisense technology, where, e.g., an antisense RNA or DNA molecule acts to block directly the translation of Expression (CRC Press: Boca Raton, FL, 1988). The oligonucleotides described above can also be delivered Another potential PRO polypeptide antagonist is an antisense RNA or DNA construct prepared using

Potential antagonists include small molecules that bind to the active site, the receptor binding site, or growth factor or other relevant binding site of the PRO polypeptide, thereby blocking the normal biological activity of the PRO polypeptide. Examples of small molecules include, but are not limited to, small peptides or peptide-like molecules, preferably soluble peptides, and symbolic non-peptidyl organic or inorganic commonate.

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Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA

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Ribozymes act by sequence-specific hybridization to the complementary target RNA, followed by endonactedyrit cleavage. Specific ribozyme cleavage sites within a potential RNA target can be identified by known techniques. For further details see, e.g., Rossi, <u>Qurrent Biology</u>, 4:469-471 (1994), and PCT publication No. WO 97/33551 (published September 18, 1997).

Nucleic acid molecules in triple-helix formation used to inhibit transcription should be single-stranded and composed of deoxynucleoides. The base composition of these oligonucleoides is designed such that it promotes triple-helix formation via Hoogsteen base-pairing rules, which generally require sizeable strenches of purines or pyrimidines on one strand of a duplex. For further details see, e.g., PCT publication No. WO 97/33551, supra.

These small molecules can be identified by any one or more of the screening assays discussed
[0] hereinabove and/or by any other screening techniques well known for those skilled in the art.

Anti-PRO Antibodies

The present invention further provides anti-PRO autibodies. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies.

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Polyclonal Antibodies

The anti-PRO antibodics may comprise polyclonal antibodies. Methods of preparing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and if desired, an adjuvant. Typically, the immunizing agent and if desired, an adjuvant. Typically, the immunizing agent in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet bemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphory) Lipid A, synthetic trebalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

Monoclonal Antibodies

The anti-PRO antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be 30 prepared using hybridoma methods, such as those described by Kohler and Milstein. Nanue, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is optically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized in vitro.

The immunizing agent will typically include the PRO polypeptide or a fusion protein thereof.

Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a

hybridoma cell [Goding, Monoclonal Antibodies; Principles and Practice, Academic Press, (1986) pp. 59-103] Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and burnan origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells tack the enzyme hypoxanibine guantine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanibine, aminopitetin, and thymidine (*HAT medium*), which substances prevent the growth of HGPRT-deficient cells.

Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of amibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Ceuter, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies [Kozbor, Linmungl., 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications. Marcel Dekker, Inc., New York, (1987) pp. 51-63].

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The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of momoclonal antibodies directed against PRO. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an in vitro binding assay, such as radioinanumnessay (RIA) or enzyme-linked immunoabsorbent assay (ELLSA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, Anal, Biochem, (07:220 (1980).

After the desired hybridoma cells are identified, the clones may be subclosed by limiting dilution procedures and grown by standard methods [Goding, supp21. Suitable culture media for this purpose include, for example, Dulbecco's Modified Engle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells may be grown in vivo as ascites in a mammal.

The monoclonal antibodies secreted by the subclunes may be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

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The monoclonal antibodies may also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4.816,557. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are espable of binding specifically to genes careoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA may be placed into expression vectors, which are then transferred into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or unyeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also may be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences [U.S. Patent No. 4.816,567; Morrison et al., <a href="https://doi.org/10.1001/10

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sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

The antibodies may be monovalent antibodies. Methods for preparing monovalent antibodies are well known in the art. For example, one method involves recombinant expression of immunoglobulin light chain and modified heavy chain. The heavy chain is truncated generally at any point in the Fc region so as to prevent heavy chain crosslinking. Alternatively, the relevant cysteine residues are substituted with another amino acid residue or are deleted so as to prevent crosslinking.

In vitro methods are also suitable for preparing monovalent antibodies. Digestion of antibodies to
10 produce fragments thereof, particularly, Fab fragments, can be accomplished using routine techniques known
in the art.

Human and Humanized Antibodies

25 20 5 Blol., 2:593-596 (1992)]. et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 322:323-329 (1988); and Presta, Qure, Op. Struct at least a portion of an immunoglobulin constant region (Fe), typically that of a human immunoglobulin [Jones those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise residues. Humanizzd antibodies may also comprise residues which are found neither in the recipient antibody species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human subsequences of antihodies) which contain minimal sequence derived from non-human immunoglobulin Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab'), or other antigen-binding The anti-PRO antibodies of the invention may further comprise humanized antibodies or human Humanized forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins

30 Mcthods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibod has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as "import" residues, which are typically taken from an 'import' variable domain. Humanization can be essentially performed following the method of Winter and co-workers [Jones et al., Nature, 321:522-525 (1986); Ricchmann et al., Nature, 322:223-327 (1988); Verhoeyen et al., Science, 329:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the

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antibodies in which some CDR residues and possibly some FR residues are substituted by residues from corresponding sequence from a non-human species. In practice, humanized antibodies are typically human analogous sites in rodent antibodies.

Ŋ (1996); Lonberg and Huxzar, Intern. Rev. Immunol., 13 65-93 (1995). which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and (1991)]. The techniques of Cole et al. and Boerner et al. are also available for the preparation of human (1994); Fishwild *et al.*, <u>Nature Biotechnology</u> <u>14</u>, 845-51 (1996); Neuberger, <u>Nature Biotechnology</u> <u>14</u>, 826 <u>Bio(Lechnology 10, 779-783 (1992); Lanberg et al., Nature 368</u> 856-859 (1994); Morrison. <u>Nature 368</u>, 812-13 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks et al. genes have been partially or completely inactivated. Upon challenge, human amibody production is observed, of human immunoglobulin loci into transgenic animals, e.g., mice in which the endagenous immunoglobulin Boetner et al., L. Immunol., 147(1):86-95 (1991)]. Similarly, human antibodies can be made by introducing display libraries [Hoogenboom and Winter, I. Mol. Biol., 227:381 (1991); Marks et al., I. Mol. Biol., 222:581 antibody tepertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; monoclonal antibodies (Cole et al., Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, p. 77 (1985) and Human antibodies can also be produced using various techniques known in the art, including phage

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Bispecific Amibodics

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PRO, the other one is for any other amigen, and preferably for a cell-surface protein or receptor or receptor specificities for at least two different untigens. In the present case, one of the binding specificities is for the Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding

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Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Trauncoker et al., EMBO pairs, where the two heavy chains have different specificities [Milstein and Cuello, Nature, 302:537-539 (1983)] Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant

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<u>1., 10</u>:3655-3659 (1991).

ಅ be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin host organism. For further details of generating bispecific antibodies see, for example, Suresh et al., Methods immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable at least one of the fusious. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the have the first heavy-chain constant region (CHI) commining the site necessary for light-chain binding present in beavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to in Enzymology, 121:210 (1986). Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can

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S size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large the yield of the heterodimer over other unwanted end-products such as homodimers. amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing replaced with larger side chains (e.g. tyrosine or tryptophan). Compensatory "cavities" of identical or similar In this method, one or more small amino acid side chains from the interface of the first antibody molecule are cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant According to another approach described in WO 96/27011, the interface between a pair of antibody

5 5 derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an cleaved to generate F(ab'), fragments. These fragments are reduced in the presence of the dithiol complexing described in the literature. For example, bispecific antibodies can be prepared can be prepared using chemical produced can be used as agents for the selective immobilization of enzymes equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies linkage. Brennan et al., Science 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab))

20 bispecific antibody $F(ab')_2$ molecule. Each Fab' fragment was separately secreted from $E.\ coli$ and subjected to directed chemical coupling in virro to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the EcbB2 receptor and normal human T cells, as well as trigger the lytic antibodies. Shalaby et al., L. Ego. Med. 175:217-225 (1992) describe the production of a fully humanized activity of human cytotoxic lymphocytes against human breast tumor targets. Fab' fragments may be directly recovered from E. coli and chemically coupled to form bispecific

25 culture have also been described. For example, bispecific antibodies have been produced using leucine zippers This method can also be utilized for the production of antibody tomodimers. The 'diabody" technology Kostelay et al., L. Immunol. 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimen Various technique for making and tsolating bispecific antibody fragments directly from recombinant cell

35 ಚ strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been described by Hollinger et al., Proc. Natl. Acad. Sci. USA 90:5444-5448 (1993) has provided an alternative two domains on the same chain. Accordingly, the V_{ii} and V_{ij} domains of one fragment are forced to pair with (V_{n}) connected to a light-chain variable domain (V_{n}) by a linker which is too short to allow pairing between the mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain reported. See, Gruber et al., L. Immunol. 152:5368 (1994). the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared

Tutt et al., J. Immunoj. 147:60 (1991).

Exemplary hispecific antibodies may bind to two different epitopes on a given PRO polypeptide herein. Alternatively, an anti-PRO polypeptide arm may be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (FeyR), such as FeyRI (CD60), FeyRI (CD32) and FeyRII (CD16) so as to focus ethilar defense mechanisms to the cell expressing the particular PRO polypeptide. Bispecific annibodies may also be used to localize cytotoxic agents to cells which express a particular PRO polypeptide. These antibodies possess a PRO-binding arm and an arm which binds a cytotoxic agent or a radiomacilide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the PRO polypeptide and further binds itsue factor (TF).

Heteroconjugate Antibodii

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Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells [U.S. Patent No. 4,676,980], and for treatment of HIV infection [WO 91/00360; WO 92/200373; EP 03089]. It is contemplated that the antibodies may be prepared in vitro using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins may be constructed using a disulfate exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptoburytimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

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Effector Function Engineering

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It may be desirable to modify the antibody of the invention with respect to effector function, so as to cultance, e.g., the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) may be introduced into the Fe region, thereby allowing interchain distilide bond formation in this region. The homodimeric antibody thus generated may have improved internalization capability and/or increased complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron et al., L

Exp. Med., 176: 1191-1195 (1992) and Shopes, L. Linmungl., 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity may also be prepared using heterobifunctional cross-linkers as described in Wolff et al. Cancer Research, 52: 2560-2565 (1993). Alternatively, an antibody can be engineered that has dual Fe regions and may thereby have enhanced complement lysis and ADCC capabilities. See Stevenson et al., Anti-Cancer Drug Design. 3: 219-220 (1989).

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Immunoconjugates

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The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (e.g., an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (i.e., a radioconjugate).

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Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above

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Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nothinding active fragments of diphtheria toxin, exotoxin A chain (from Pseudononas aeruginosa), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, Aleurites fordii proteins, dianthin proteins, Physolaca americana proteins (PAPI, PAPII, and PAPS), monordica charantia inhibitor, currein, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictorin, phenomycin, enomycin, and the tricothecenes. A variety of radiomelides are swallable for the production of radioconjugated amibodica. Examples include: 113ji, 131, 131n, 131n, 132, and 134cc.

Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridylulthiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), acrive esters (such as disuccinimidyl suberate), addehydes (such as glutaretdehyde), bis-azido compounds (such as bis (p-uzidobenzoyl) heranodiamino), bis-didezonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diitocyanates (such as tolyene 2,6-dilitocyanate), and bis-acrive fluorine compounds (such as 1,5-difhoto-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta et al., Science, 238: 1098 (1987). Carbon-14-labeled 1-isoxbiocyanatobenzyl-3-methyldiethylene triaminepentanectic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radiomucleotide to the amibody. See WO94/11025.

In another embodiment, the antibody may be conjugated to a "receptor" (such strepavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound emjugate from the circulation using a clearing agent and then administration of a "ligand" (e.g., a vidin) that is conjugated to a cytotoxic agent (e.g., a radionucleoxide).

8. <u>Immunoliposome</u>

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The antibodies disclosed herein may also be formulated as immunoliposomes. Liposomes containing the antibody are prepared by methods known in the art, such as described in Epstein et al., Proc. Natl. Acad. Sci. USA, 27: 4030 (1980); and U.S. Pat. Nos. 4,485,045 and 4,544,545. Liposomes with enhanced circulation time are disclosed in U.S. Patent No. 25 5,013,556.

Particularly useful liposomes can be generated by the reverse-phase evaporation method with a lipid composition comprising phosphatidyleholine_cholesterol, and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired diameter. Fab' fragments of the antibody of the present invention can be conjugated to the liposomes as described in Martin 30 et al., <u>J. Biol. Chem.</u> 257: 286-288 (1982) via a disulfide-interchange reaction. A chemotherapeutic agent (such as Doxorubicia) is optionally contained within the liposome. See Gabizon et al., <u>J. National Cancer Inst.</u> 81(199): 1484 (1989).

Pharmaceutical Compositions of Antibodies

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Antibodies specifically binding a PRO polypeptide identified berein, as well as other moleculer identified by the screening assays disclosed hereinbefore, can be administered for the treatment of various disorders in the form of pharmaceutical compositions.

If the PRO polypeptide is intracellular and whole anibodies are used as inhibitors, internalizing anibodies are preferred. However, lipofections or liposomes can also be used to deliver the anibody, or an anibody fragment, into cells. Where anibody fragments are used, the smallest inhibitory fragment that specifically hinds to the binding domain of the target protein is preferred. For example, based upon the variable-region sequences of an anibody, peptide molecules can be designed that retain the ability to bind the target protein sequence. Such peptides can be synthesized chemically anidor produced by recombinant DNA technology. See, e.g., Marasco et al., Proc., Nall., Acad., Sci., USA, 20: 7889-7893 (1993). The formation herein may also contain more than one active compound as necessary for the particular indication being treated, preferably those with complementary activities that do not adversely affect each other. Alternatively, or in addition, the composition may comprise an agent that enhances its function, such as, for example, a cytotoxic agent, cytokine, chemotherapeutic agent, or growth-inhibitory agent. Such molecules are suitably present in combination in amounts that are effective for the purpose intended.

The active ingredients may also be entrapped in microcapsules prepared, for example, by concervation techniques or by interfacial polymerization, for example, hydroxymethylocallulose or gelatin-microcapsules and poly-fmethylmethacylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microcamulsions, nano-particles, and nanocapsules) or in macrocamulsions. Such techniques are disclosed in Remington's <u>Pharmaceutical Sciences</u>, supra.

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The formulations to be used for in vivo administration must be sterile. This is readily accomplished by filtration through sterile filtration membrancs.

30 23 8 mechanism is discovered to be intermolecular S-S bond formation through thio-distulfide interchange, stabilization can be devised for stabilization depending on the mechanism involved. For example, if the aggregation microspheres composed of lactic acid-glycolic acid copolymer and leaprolide acetate), and poly-D-(-)-3include semipermeable matrices of solid hydrophobic polymers containing the antibody, which matrices are in at 37°C, resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies antibodies remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture of molecules for over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated hydroxybutyric acid. While polymers such as ethylene-vinyl acetate and factic acid-glycolic acid enable release (U.S. Pat. No. 3,773,919), copolymers of Leglutamic acid and y ethyl-Leglutamate, non-degradable ethylenepolyecters, bydrogets (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylateohol)), polylactides content, using appropriate additives, and developing specific polymer matrix compositions may be achieved by modifying sulfaydryl residues, lyophilizing from acidic solutions, controlling moisture vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the LUPRON DEPOT TM (injectable the form of shaped articles, e.g., films, or microcapsules. Examples of sustained-release matrices include Sustained-release preparations may be prepared. Suitable examples of sustained-release preparations

G. Uses for anti-PRO Antibodies

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The ami-PRO amibodies of the invention have various utilities. For example, ani-PRO amibodies may be used in diagnostic assays for PRO, e.g., detecting its expression in specific cells, tissues, or serum. Various

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diagnostic assay techniques known in the art may be used, such as competitive binding assays, direct or indirect sandwitch assays and immunoprecipitation assays conducted in either heterogeneous or homogeneous phases [204a, Monoclonal Antibodies; A.Manual of Techniques, CRC Press, Inc. (1987) pp. 147-158]. The antibodies used in the diagnostic assays can be labeled with a detectable moiety. The detectable moiety should be capable of producing, either directly or indirectly, a detectable signal. For example, the detectable moiety may be a radioistotope, such as 'H, '*C, F*P, *S*, or 'F*I, a fluoresecut or chemituminescent compound, such as fluoresecutionisothopy anate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactoridate or horseradiah peroxidase. Any method known in the art for conjugating the antibody to the detectable molety may be employed, including those methods described by Hunter et al., Nanue, 144:945 (1963); David et al., Biochemistry, 12:1014 (1974); Pain et al., L.Immunol, Meth., 40:219 (1981); and Nygron, L.Histochem, and Cytochem, 30:407 (1982).

Anti-PRO antibodies also are useful for the affinity purification of PRO from recombinant cell culture or natural sources. In this process, the antibodies against PRO are immobilized on a suitable support, such a Sephadex resin or filter paper, using methods well known in the art. The immobilized antibody then is contacted with a sample containing the PRO to be purified, and thereafter the support is washed with a suitable solvent that will remove substantially all the material in the second access to the

15 will remove substantially all the material in the sample except the PRO, which is bound to the immobilized antibody. Finally, the support is washed with mother suitable solvent that will release the PRO from the antibody.

The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

20 All patent and literature references clied in the present specification are hereby incorporated by references in their entirety.

EXAMPLES

Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, Manassas, VA.

EXAMPLE 1: Extracellular Domain Humology Screening to Identify Novel Polypeptides and cDNA Encoding. Therefore

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The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proxetus from the Swiss-Prox public database were used to search EST databases. The EST databases included public databases (e.g., Dayboff, GenBank), and proprietary databases (e.g., LIFESEQT¹⁴, Incyre Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or

35 BLAST-2 (Altschul et al., Methods in Enzymology, 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons with a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA.

sequences with the program "phrap" (Phil Green, University of Washington, Scattle, WA).

Using this extracellular domain bomology screen, consensus DNA sequences were assembled relative to the other identified EST sequences using phrap. In addition, the consensus DNA sequences obtained were often (but not always) extended using repeated cycles of BLAST or BLAST-2 and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above.

Based upon the consensus sequences obtained as described above, oligonucleoxides were then synthesized and used to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for a PRO polypeptide. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional 100 oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to series several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Prosocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones exceeding the gene of interest using the probe oligonucleotide and one of the primer pairs.

The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Dlego, CA. The cDNA was primed with odigo dT containing a Notl site, linked with blunt to Sall hemblinased adaptors, cleaved with Notl, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRKSB is a precursor of pRKSD that does not commin the Sfil site; see, Holmes et al., Science, 253:1276-1280 (1991)) in the unique Xhol and Notl sites.

EXAMPLE 2: Isolation of cDNA clones by Amylase Screening

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Preparation of olige dT primed cDNA library

mRNA was isolated from a human tistue of interest using reagents and protocols from Invitrogen, San Diego, CA (Fast Track 2). This RNA was used to generate an oligo dT primed cDNA library in the vector pRK5D using reagents and protocols from Life Technologies, Gaithersburg, MD (Super Script Plasmid System). In this procedure, the double stranded cDNA was sized to greater than 1000 by and the Sall/Notl linkered cDNA was closed into Xhol/Notl cleaved vector. pRK5D is a closing vector that has an sp6 transcription initiation site followed by an Sfil restriction enzyme site proceeding the Xhol/Notl cDNA cloning sites.

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Preparation of random primed cDNA library

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A secondary cDNA library was generated in order to preferentially represent the S' ends of the primary cDNA clones. Sp6 RNA was generated from the primary library (described above), and this RNA was used to generate a rundom primed cDNA library in the vector pSST-AMY.0 using reagents and protocols from Life Technologies (Super Script Plasmid System, referenced above). In this procedure the double stranded cDNA was sized to 500-1000 bp, linkered with blunt to Notl adaptors, cleaved with Sfil, and cloned into Sfil/Notl cleaved vector. pSST-AMY.0 is a cloning vector that has a yeast alcohol dehydrogenase promoter preceding the cDNA cloning sites and the mouse anythes sequence (the mature sequence without the secretion signal)

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followed by the yeast alcohol dehydrogenase terminator, after the cloning sites. Thus, cDNAs cloned into this vector that are fused in frame with amylase sequence will lead to the secretion of amylase from appropriately transferred yeast colonies.

Transformation and Detection

DNA from the library described in paragraph 2 above was chilled on ice to which was added electrocompetent DH10B bacteria (Life Technologies, 20 ml). The bacteria and vector mixture was then electroporated as recommended by the manufacturer. Subsequently, SOC media (Life Technologies, 1 ml) was added and the mixture was incubated at 37°C for 30 minutes. The transformants were then plated onto 20 standard 150 mm LB plates containing ampleillin and incubated for 16 hours (37°C). Positive colonies were 10 scraped off the plates and the DNA was isolated from the bacterial pellet using standard protocols, e.g. C3C1-

The yeast methods were divided into three categories: (1) Transformation of yeast with the plasmid/cDNA combined vector; (2) Detection and isolation of yeast clones secreting amylase; and (3) PCR amplification of the insert directly from the yeast colony and purification of the DNA for sequencing and further

gradient. The purified DNA was then carried on to the yeast protocols below.

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The yeast strain used was HDS6-5A (ATCC-90785). This strain has the following genotype: MAT alpha, ural-52, leu2-3, leu2-112, his3-11, his3-15, MAL*, SUC*, GAL*. Preferably, yeast minimus can be employed that have deficient post-translational pathways. Such mutants may have translocation deficient alleles in sec71, sec72, sec62, with truncated sec71 being most preferred. Alternatively, anagonists (including antisense nucleorides and/or tigands) which interfere with the normal operation of these genes, other proteins implicated in this post translation pathway (e.g., SEC61p, SEC72p, SEC62p, SEC63p, TDJ1p or SSA1p-4p) or the complex formation of these proteins may also be preferably employed in combination with the amylase-expressing years.

25 (1992). Transformation was performed based on the protocol outlined by Gietz et al., Nucl. Acid. Res., 20:1425
(1992). Transformed cells were then inoculated from agar into YEPD complex media broth (100 ml) and grown overnight at 30°C. The YEPD broth was prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 207 (1994). The overnight culture was then dibated to about 2 x 10⁶ cells/ml (approx. OD₆₀₀=0.1) into fresh YEPD broth (500 ml) and regrown to 1 x 10⁶ cells/ml (approx. OD₆₀₀=0.4-0.5).

30 The cells were then harvested and prepared for transformation by transfer imto GS3 rotor bottles in a Sorval GS3 rotor at 5,000 rpm for 5 minutes, the supernatural discarded, and then resuspended into sterile water, and cemrifuged again in 50 ml falcon tubes at 3,500 rpm in a Bockman GS-6KR cemrifuge. The supernatural was discarded and the cells were subsequently washed with LIAC/TE (10 ml, 10 mM Tris-HCl, 1 mM EDTA pH 7.5, 100 mM LI₂OOCCH₃), and resuspended into LIAC/TE (2.5 ml).

35 Transformation took piece by mixing the prepared cells (100 µl) with freshly denatured single stranded salmon testes DNA (Lofstrand Labs, Galthersburg, MD) and transforming DNA (1 µg, vol. < 10 µl) in microfuge tubes. The mixture was mixed briefly by vortexing, then 40% PEG/TE (600 µl, 40% polyethylene

were then diluted into TE (1 ml) and aliquots (200 µl) were spread onto the selective media previously prepared for 15 minutes, and the reaction vessel centrifuged in a microfuge at 12,000 rpm for 5-10 seconds, decanted and resuspended into TE (300 μ l, 10 mM Tris-HCl, 1 mM EDTA pH 7.5) followed by recentrifugation. The cells gently mixed and incubated at 30°C while agitating for 30 minutes. The cells were then heat shocked at 42°C glycol-4000, 10 mM Tris-HCl, 1 mM EDTA, 100 mM Ll;00CCH₃, pH 7.5) was added. This mixture was

scale reaction, wherein reagent amounts were scaled up accordingly. Alternatively, instead of multiple small reactions, the transformation was performed using a single, large S

208-210 (1994). Transformants were grown at 30°C for 2-3 days. described in Kaiser et al., <u>Methods in Yeast Genetics</u>, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. The selective media used was a synthetic complete dextrose agar lacking uracii (SCD-Ura) prepared as

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100 mM final concentration). plates at a final concentration of 0.15% (w/v), and was buffered with potassium phosphate to a pH of 7.0 (50-Biely et al., Anal. Biochem., 172:176-179 (1988). The coupled starch was incorporated into the SCD-Ura agar growth media. Starch was coupled to the red dye (Reactive Red-120, Sigma) as per the procedure described by The detection of colonies secreting anylase was performed by including red starch in the selective

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determined by their ability to break down starch resulting in a clear halo around the positive colony visualized secretion were detected by direct incorporation of red starch into buffered SCD-Ura agar. Positive colonies were order to obtain well isolated and identifiable single colonies. Well isolated single colonies positive for amylase The positive colonics were picked and streaked across fresh selective media (omo 150 mm places) in

Isolation of DNA by PCR Amplification

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analysis or immediately amplified. An aliquor of cells (5 μl) was used as a template for the PCR reaction in a Cetus); 2.5 µl Kennaq buffer (Clonnech); 0.25 µl forward oligo 1; 0.25 µl reverse oligo 2; 12.5 µl distilled water 25 μl volume containing: 0.5 μl Klentaq (Clontech, Palo Alto, CA); 4.0 μl 10 mM dNTP's (Perkin Elmer-The sequence of the forward oligonucleotide I was: water (30 µI) in a 96 well plate. At this time, the positive colonies were either frozen and stored for subsequent When a positive colony was isolated, a portion of it was picked by a toothpick and diluted into sterile

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The sequence of reverse oligonucleotide 2 was: 5'-TGTAAAACGACGGCCAGTTAAATAGACCTGCAATTATTAATCT-3' (SEQ ID NO:1)

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5'-CAGGAAACAGCTATGACCACCTGCACACCTGCAAATCCATT-3' (SEQ ID NO:2) PCR was then performed as follows:

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3 cycles of:	3 cycles of:	
Denature Anneal	Denature Anneal Extend	Denature
92°C. 57°C.	92°C, 72°C,	92°C,
30 seconds 30 seconds	30 seconds 30 seconds 60 seconds	5 minutes

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9	.	
	25 cycles of:	
Hold	Denature Anneal Extend	Extend
4°C	25.C. 25.C.	72°C.
	30 seconds 30 seconds 60 seconds	60 seconds

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5 Typically, the first 18 nucleotides of the 5' end of these oligonucleotides contained annealing sites for the signal sequence-fused cDNA resulted in considerably longer nucleoside sequences. sequencing primers. Thus, the total product of the PCR reaction from an empty vector was 343 bp. However, region, respectively, and amplified a 307 bp region from vector pSST-AMY.0 when no insert was present The underlined regions of the oligonucleotides annealed to the ADH promoter region and the arrylass

5 a 1% agarose gel using a Tris-Borate-EDTA (TBE) buffering system as described by Sambrook et al., supra. Clones resulting in a single strong PCR product larger than 400 hp were further analyzed by DNA sequencing after purification with a 96 Qiaquick PCR clean-up column (Qingen Inc., Chaisworth, CA). Following the PCR, an aliquot of the reaction (5 µl) was examined by agarose gel electrophoresis in

EXAMPLE 3: Isolation of cDNA Clones Using Signal Algorithm Analysis

30 ß 20 in the identification of numerous polypeptide-encoding nucleic acid sequences. following the first ATG must code for at least 35 mambiguous amino acids without any stop codons. If the first sequence is not scored. In order to determine whether the EST sequence contains an authentic signal sequence, sequence finding algorithm developed by Generatech, Inc. (South San Francisco, CA) upon ESTs as well as sensors (evaluation parameters) known to be associated with secretion signals. Use of this algorithm resulted the DNA and corresponding amino acid sequences surrounding the ATG codon are scored using a set of seven ATG has the required amino acids, the second is not examined. If neither meets the requirement, the candidate codum(s) (ATG) at the 5'-end of the sequence or sequence fragment under consideration. The nucleotides clustered and assembled EST fragments from public (e.g., GenBank) and/or private (LIFESEQ®, Incyto score based on the character of the DNA nucleotides surrounding the first and optionally the second methionine Pharmaceuticals, Inc., Palo Alto, CA) databases. The signal sequence algorithm computes a secretion signal Various polypeptide-encoding nucleic acid sequences were identified by applying a proprietary signal

EXAMPLE 4: Isolation of cDNA clones Encoding Human PRO1560

35 consensus sequence, oligonucleotides were synthesized: () to identify by PCR a cDNA library that contained in Example 1 above. This consensus sequence is designated herein as DNA17409. Based on the DNA17409 the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

8 for DNA19902-1669 [Figure 1, SEQ ID NO:3]; and the derived protein sequence for PRO1560. DNA sequencing of the isolated clones isolated as described above gave the full-length DNA sequence

The entire coding sequence of DNA19902-1669 is included in Figure 1 (SEQ ID NO:3). Clone

DNA 19902-1669 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 41-43, and an apparent stop codon at nucleotide positions 776-778. The predicted polypeptide precursor is 245 amino acids long. The approximate locations of the signal peptide, transmembrane domains, N-glycosylation sites, N-myristoylation sites, tyrosine binase phosphorylation sites, and membrane lipoprotein lipid attachment sites are also indicated in Figure 2. Clone DNA 19902-1669 has been deposited with the ATCC and is assigned ATCC deposit no. 203454. The full-length PRO1560 protein shown in Figure 2 has an estimated molecular wright of about 21,563 dattons and a p1 of about 8.36.

An analysis of the Dayhoff danabase (version 35.45 SwissProx 35), using a WU-BLASTZ sequence alignment analysis of the full-length sequence shown in Figure 2 (SEQ ID NO.4), revealed sequence identify between the PRO1560 amino acid sequence and the following Dayhoff sequencess: AF053452_1, AF053454_1, A1611MAN AFN68801 | CPCS HILLAN ASSESSED | AF053452_1, AF053454_1, A1611MAN AFN68801 | CPCS HILLAN ASSESSED | AF053452_1, AF053454_1, A1611MAN AFN68801 | CPCS HILLAN ASSESSED | AF053452_1, AF053454_1, A1611MAN AFN68801 | CPCS HILLAN ASSESSED | AF054803 | AF054803 | AFN68801 | CPCS HILLAN ASSESSED | AF054803 | AFN68801 |

10 A15_HUMAN, AF054840_1, CD63_HUMAN, AF063389_1, AF054838_1, AF089749_1, P_R27525, and P_R86834.

EXAMPLE 5: Isolation of cDNA clones Encoding Human PRO444

A cDNA sequence isolated in the amylase screen described in Example 2 above was designated

15 DNA13121. Based upon this sequence, probes were generated and used to screen a human fetal lung library

(LIR25) prepared as described in paragraph 1 of Example 2 above. The cloning vector was prK5B (prK5B

is a precursor of prK5D that does not comain the SfU site; see, Holmes et al., <u>Science</u>, <u>253</u>:1278-1280 (1991)),

and the cDNA size cut was less than 2800 bp.

A full length clone was identified that contained a single open reading frame with an apparent 20 translational initiation site at mucleotide positions 608-610 and ending at the stop codon found at nucleotide positions 939-961 (Figure 3, SEQ ID NO:5). The predicted polypeptide precursor is 117 amino acids long, has a calculated molecular weight of approximately 12,692 daltons and an estimated pl of approximately 7.50. Analysis of the full-length PRO444 sequence shown in Figure 4 (SEQ ID NO:6) evidences the presence of a signal peptide at amino acid 1 to about amino acid 16. An analysis of the Dayhoff database (version 35.45 SwitsProt 35) evidenced bomology between the PRO444 amino acid sequence and the following Dayhoff sequences: CEF44D112.8, P_R88452, YNE1_CAEEL, A47312, AF009957_1, and A06133_1. Clone DNA26846-1397 was deposited with the ATCC on October 27, 1998 and is assigned ATCC deposit no. 203406.

EXAMPLE 6: Isolation of cDNA clones Encoding Human PRO1018

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A cDNA clone (DNA56107-1415) encoding a native human PRO1018 polypeptide was identified by a yeast screen, in a human ovary unmor cDNA library that preferentially represents the 5' ends of the primary cDNA clones. The yeast screen employed identified a single EST clone designated herein as DNA41000. The DNA41000 ecquence was then compared to various EST databases including public EST databases (e.g., Genhank), and a proprietary EST database (LHFESEQ*, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparisons was performed using the computer program BLAST or BLAST of [Altschul et al., Methods in Emzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into

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a consensus DNA sequence with the program 'phrap' (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA44449. Oligonsucleotide primers based upon the DNA44449 sequence were then synthesized and employed to screen a human ovary numor cDNA library which resulted in the identification of the DNA56107-1415 close shown in Figure 5.

The full-length DNA56107-1415 clone shown in Figure 5 contains a single open reading frame with 5 an apparent translational initiation site at nucleotide positions 129-131 and ending at the stop codon at nucleotide positions 696-698 (Figure 5). The predicted polypeptide precursor is 189 amino acids long (Figure 5). Analysis of the full-length PRO1018 sequence shown in Figure 6 (SEQ ID NO:8) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, transmembrane domains from about amino acid sequence 86 to about amino acid 103 and from about amino acid 60 to about amino acid 175 and an amino acid sequence

block having homology to G-protein coupled receptor proteins from about amino acid 44 to about amino acid
 Close DNA56107-1415 has been deposited with ATCC on October 27, 1998 and is assigned ATCC deposit no. 203405.

An analysis of the Dayholf database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 6 (SEQ ID NO:8), evidenced significant 15 homology between the PRO1018 amino ucid sequence and the following Dayhoff sequences: CEB0399_4, S59764, VHDT_HAEIN and AE000675_3.

EXAMPLE 7: Isolation of cDNA clones Encoding Human PRO1773

A consonsus DNA sequence was assembled relative to other BST sequences using phrap as described

20 in Example 1 above. This consensus sequence is herein designated DNA49797. Based upon an observed
homology between the DNA49797 consensus sequence and an EST sequence contained within lacyto EST clone
no. 509434, Incyte EST clone no. 509434 was purchased and its insert obtained and sequenced. That sequence
is herein shown in Figure 7 and is designated DNA56406-1704.

Š 30 25 acid 47, from about amino acid 108 to about amino acid 113, from about amino acid 166 to about amino acid from about amino acid 1 to about amino acid 17, a transmembrane domain from about amino acid 136 to about 8 has an estimated molecular weight of about 35,227 daitons and a pt of about 8.97. Analysis of the full-length DNA56406-1704 comains a single open reading frame with an apparent translational initiation site at nucleotide 212. Clone DNA56406-1704 has been deposited with ATCC on November 17, 1998 and is assigned ATCC 171, from about amino acid 198 to about amino acid 203 and from about amino acid 207 to about amino acid myristolation sites from about amino acid 36 to about amino acid 41, from about amino acid 42 to about amino glycosaminoglycan attachment site from about amino acid 39 to about amino acid 42 and potential Namino acid 187 to about amino acid 190 and from about amino acid 253 to about amino acid 256, a amino acid 152, potential N-glycosylation sites from about amino acid 161 to about amino acid 164, from about PRO1773 sequence shown in Figure 8 (SEQ ID NO:10) evidences the presence of the following: a signal peptide polypeptide precursor is 319 amino acids long (Figure 8). The full-length PRO1773 protein shown in Figure positions 111-113 and ending at the stop codon at nucleotide positions 1068-1070 (Figure 7). The predicted The entire nucleoride sequence of DNA56406-1704 is shown in Figure 7 (SEQ ID NO:9). Clone

deposit no. 203478.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WIJ-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 8 (SEQ ID NO:10), evidenced significant homology between the PRO1773 amino acid sequence and the following Dayhoff sequences: ROH2_RAT, ROH3_RAT, AF030513_1, ROH1_RAT, AF056194_1, AF057034_1, P_W18337, P_W18228, BDH_HUMAN and BDH_RAT.

EXAMPLE 8: Isolation of cDNA clones, Encoding Human PRO1477.

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA52641. Based on the DNA52641 consensus sequence, oligonucleotides were synthetized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for

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PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CGCCAGAAGGGCGTGATTGACGTC-3' (SEQ ID NO:13)

reverse PCR primer 5'-CCATCCTTCCTTCCCCAGACAGGCCG-3' (SEQ ID NO:14)

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Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNAS2641 sequence which had the following nucleotide sequence:

S'-GAAGCCTGTGTCCAGGTCCTTCAGTGAGTGGTTTGGCCTCGGTC-3' (SEQ ID NO:15)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO240 gene using the probe oligonuclootide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1477 (designated herein as DNA56529-1647 [Figure 9, SEQ ID NO:11]; and the derived protein sequence for PRO1477.

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The entire nucleotide sequence of DNA56529-1647 is shown in Figure 9 (SEQ ID NO:11). Clone DNA56529-1647 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 23-25 and ending at the stop codon at nucleotide positions 2120-2122 (Figure 9). The predicted polypeptide precursor is 699 aminu acids long (Figure 10). The full-length PRO240 protein shown in Figure 10 has an estimated modecular weight of about 79.553 dattons and a p1 of about 7.83. Analysis of the full-length

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PRO1477 sequence shown in Figure 10 (SEQ ID NO:12) evidences the presence of the following: uransumernbrane domains from about amino acid 21 to about amino acid 40 rad from about amino acid 84 to about amino acid 105. Clone DNA56539-1647 has been deposited with ATCC on September 29, 1998 and is assigned ATCC deposit no. 203393.

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An analysis of the Dayboff dasabase (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 10 (SEQ ID NO:12), erdenced significant

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homology between the PRO1477 amitro acid sequence and the following Dayhoff sequences: CELT03G11_1, CEZC410_4, A54408, SSMAN9MAN_1, GEN12643, GEN12642, AF0Z7156_1, P_W46900, SPAC23A1_4 and DMC86E4_5.

EXAMPLE 9: Isolation of cDNA clones Encoding Illuman PRO1478

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "DNASZ719". Based on the DNASZ719 consensus sequence, oligomucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1478.

PCR primers (forward and reverse) were synthesized:

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forward PCR primer 5'GCGAACGCTTCGAGGAGTCCTGG3' (SEQ ID NO:18); and

reverse PCR primer S'GCAGTGCGGGAAGCCACATGGTAC3' (SEQ ID NO:19).

Additionally, a synthetic oligonucleoxide hybridization probe was constructed from the consensus DNA52719 sequence which had the following nucleotide sequence:

15 <u>bybidization probe</u> S'CTTCCTGAGCAGGAAGAAGATCCGGCACCACCATCTACGTGCTCAAC3'(SEQ ID NO;20).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1478 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

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DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1478 and the derived protein sequence for PRO1478.

The entire coding sequence of PRO1478 is included in Figure 11 (SEQ ID NO:16). Clone DNA565311648 contains a single open reading frame with an apparent translational initiation site at nucleotide positions
25 77-79 and an apparent stop codon at nucleotide positions 1058-1060 of SEQ ID NO:16. The predicted
polypeptide precursor is 327 amino acids long. The type II transmembrane sequence is believed to be at about
amino acids 29-49 of SEQ ID NO:17, and an N-glycosylation site is believed to be at about amino acids 154-157
of SEQ ID NO:17. Clone DNA56531-1648 has been deposited with ATCC and is assigned ATCC deposit no.
203286. The full-length PRO1478 protein shown in Figure 12 has an estimated molecular weight of about 9.3.

An analysis of the Dayboff database (version 35.45 SwissProi 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 12 (SEQ ID NO:17), revealed sequence identify between the PRO1478 amino acid sequences and the following Dayhoff sequences: YNI4_CAEEL, P_RS5706, A38781_1, NALS_MOUSE, HUMHGT_1, AF048687_1, CEW02B12_11, Y09F_MYCTU, FOJO_DROME, and G01936.

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EXAMPLE 10: Isolation of cDNA clones Encoding Human PRO831

DNA56862-1343 was identified by applying the proprietary signal sequence finding algorithm described in Example 3 above. Use of the above described signal sequence algorithm allowed identification of an EST cluster sequence from the heyte database, designated lacyte cluster sequence no. 25507. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq*, Incyte Pharmacetuicals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Attabul et al., Methods, in Enzymology, 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington).

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In light of the sequence homology between the DNA55714 sequence and an EST sequence contained within the Merck EST clone no. AA099445, the Merck EST clone no. AA099445 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 13 and is herein designated as DNA56862-1343.

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The consensus sequence obtained therefrom is herein designated as DNASS714.

Clone DNA56862-1343 contains a single open reading frame with an apparent translational initiation inte at nucleoside positions 40-42 and ending at the stop codon at nucleoside positions 259-261 (Figure 13). The predicted polypoptide precursor is 73 amino acids long (Figure 14). The full-length PRO831 protein shown in Figure 14 has an estimated molecular weight of about 7.879 dations and a pt of about 7.21. Analysis of the full-length PRO831 sequence shown in Figure 14 (SEQ ID NO:22) evidences the presence of the following: a signal 20 peptide from about amino acid 10 about amino acid 10 about amino acid 30 about amino acid 18. Clone DNA56862-1343 has been deposited with ATCC on September 1, 1998 and is assigned ATCC deposit no.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence 25 alignment analysis of the full-length sequence shown in Figure 14 (SEQ ID NO:22), evidenced significant homology between the PRO831 amino acid sequence and the following Dayhoff sequences: P_W30724, HUMPPA_I,AF022238_I,4HHB_C,P_R39727,P_R39728,TRYT_MERUN, GPR5_HUMAN, AB010266_3 and HSBCL352_1.

30 EXAMPLE 11: Isolation of cDNA clones Encoding Human PRO1113

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "DNA34025". Based on the DNA34025 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1113.

PCR primers (forward and reverse) were synthesized:

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forward.PCR primer 5'GAGGACTCACCAATCTGGTTCGGC3' (SEQ ID NO:25); and

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reverse PCR primer 5'AACTGGAAAGGAAGGCTGTCTCCC3' (SEQ ID NO:26).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA34025 sequence which had the following nucleotide sequence:

NOBIGIZATION PRODE S'GTAMAGGAGAAGAACATCACGGTACGGGATACCAGGTGTGTTTATCCTAA3 (SEQ ID NO:27).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1113 gene using the probe ollgometeotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for 10 PRO1113 (designated herein as DNA57254-1477 [Figure 13, SEQ ID NO:23]; and the derived protein sequence for PRO1113.

The entire coding sequence of PRO1113 is shown in Figure 15 (SEQ ID NO:23). Clone DNA572541477 contains a single open reading frame with an apparent translational initiation site at nucleotide positions
214-216, and an apparent stop codon at nucleotide positions 2062-2064 of SEQ ID NO:23. The predicted
5 polypoptide precursor is 616 amino acids long. The transmembrane domain (type II) is believed to be at about
amino acids 13-40 of SEQ ID NO:24. The N-glycosylation sites and N-mynistoylation sites are indicated in

13 polypoptide precursor is 616 amino acids long. The transmembrane domain (type II) is believed to be at about amino acids 13-40 of SEQ ID NO:24. The N-glycosylation sites and N-myristoylation sites are indicated in Figure 16. Clone DNA57254-1477 has been deposited with the ATCC and is assigned ATCC deposit no. 203289. The full-length PRO1113 protein shown in Figure 16 has an estimated molecular weight of about 68,243 dahcurs and a pl of about 8,66.

An analysis of the Dayloff database (version 34.45 Suite-Dom 34.5) writes a turn to a com-

O An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLASTZ sequence alignment analysis of the full-length sequence shown in Figure 16 (SEQ ID NO:24), revealed sequence identity between the PRO1113 amino acid sequence and the following Dayhoff sequences (data incorporated herein): D86983_1, A38532, SLIT_DROME, AB007865_1, AC004142_1, CELTZ1D12_8, AB003184_1, DMU4Z767_1, MUSLRRP_1 and GPCR_LYMST.

EXAMPLE 12: Isolation of cDNA clones Encoding Human PRO1194

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., OmBank) and a proprietary

30 EST DNA database (LIFESEQ*, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing bomologies. One or more of the ESTs was derived from a human pineal gland library. The homology search was performed using the computer program BLAST or BLAST2 (Altahul et al., Meshods in Enzymology 256,460-480 (1996)). Those computions resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington). Seattle, Washington). The consensus sequence obtained therefrom is herein

In light of the sequence homology between the DNAS6511 sequence and an EST contained within the

designated DNA56511.

obtained and sequenced. The sequence of this cDNA insert is shown in Figure 17 and is herein designated as Merck EST AA069568, the clone 382736 which includes this EST was purchased and the cDNA insert was

DNA57841-1522 was deposited with the ATCC on November 3, 1998 and is assigned ATCC deposit no molecular weight of approximately 9,223 dations and an estimated pl of approximately 10.47. Clone amino acids long. The signal peptide is at about artino acids 1-21 of SEQ ID NO:29. PRO1194 has a calculated 252-254 (Figure 17; SEQ ID NO:28). The predicted polypeptide precursor (Figure 18, SEQ ID NO:29) is 81 (ranslational initiation site at nucleotide positions 9-11 and ending at the stop codon found at nucleotide positions The full length clone shown in Figure 17 contained a single open reading frame with an apparen

5 RR2_CHLVU, CEK12F2_1, S22452, S76705, AF031898_7, A4_DROME, AF038931_1, E49905, and between the PRO1194 amino acid sequence and the following Dayhoff sequences: PT17_YEAST alignment analysis of the full-length sequence shown in Figure 18 (SEQ ID NO:29), revealed sequence identity An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

EXAMPLE 13: Isolation of cDNA clones Encoding Human PRO1110.

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23 20 a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, DNA45566 sequence was then compared to various EST databases including public EST databases (e.g., cDNA library (LIB247) which resulted in the identification of the DNAS8727-1474 clone shown in Figure 19. the DNA4696S sequence were then synthesized and employed to screen a human SK-Lu-1 adeoocarcinoma of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score Washington). This consensus sequence is herein designated DNA46965. Oligonucleotide primers based upon bomologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 GcnBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to Identify cDNA clones. The yeast sorten employed identified a single EST clone designated herein as DNA45566. The a yeast secreen, in a human fetal kidney cDNA library that preferentially represents the 5' ends of the primary A cDNA clone (DNA58727-1474) encoding a native human PRO1110 polypeptide was identified by

35 30 an apparent translational initiation site at nucleotide positions 131-133 and ending at the stop codon at nucleotide 60, from about amino acid 66 to about amino acid 85, from about amino acid 101 to about amino acid 120, from a pl of about 8.57. Analysis of the full-length PRO1110 sequence shown in Figure 20 (SEQ ID NO:31) about amino acid 137 to about amino acid 153, from about amino acid 171 to about amino acid 192, from about positions 1097-1099 (Figure 19). The predicted polypeptide precursor is 322 amino acids long (Figure 20). The evidences the presence of the following: transmembrane domains from about amino acid 41 to about amino acid full-length PRO1110 protein shown in Figure 20 has an estimated molecular weight of about 35,274 daltons and The full-length DNAS8727-1474 clone shown in Figure 19 contains a single open reading frame with

amino acid 205 to about amino acid 226, from about amino acid 235 to about amino acid 255 and from about

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DNA58727-1474 has been deposited with ATCC on September 1, 1998 and is assigned ATCC deposit no. acid 69, and a glycosaminoglycan attachment site from about amino acid 18 to about amino acid 21. Cloru amino acid 294 to about amino acid 312, a potential N-glycosylation site from about amino acid 6 to about amine

alignment analysis of the full-length sequence shown in Figure 20 (SEQ ID NO:31), evidenced significant P_R99799, MAL_HUMAN. P_P80929, RNMALGENE_1, S68406, PLLP_RAT, MMMALPROT_1, I38891 homology between the PRO1110 amino acid sequence and the following Dayhoff sequences: MMMYELUPR_1, An analysis of the Dayhoff database (version 35,45 SwissProt 35), using a WU-BLAST2 sequence

70 EXAMPLE 14: Isolation of cDNA clones Encoding Human PRO1378

of the full-length coding sequence for PRO1377 from a hone marrow cDNA library: on the DNAS 1941 sequence, the following oligonucleotides were synthesized for use as probes to isolate a clone human bone marrow cDNA library that preferentially represents the 5° ends of the primary cDNA clones. Based An initial DNA sequence referred to herein as DNAS1941 was identified using a yeast screen, in a

- TGTCCTTTGTCCCAGACTTCTGTCC (SEQ ID NO:37); GGAGATCGCTGCGCTGGCCAGGTCCTCCCTGCATGGTAT (SEQ ID NO:38); and TTCCACTCAATGAGGTGAGCCACTC (SEQ ID NO:36); GGCGAGCCCTAACTATCCAGGAG (SEQ ID CTGGATGCTAATGTGTCCAGTAAATGATCCCCCTTATCCCGTCGCGATGCT (SEQ ID NO:35); CTGCTGCAAAGCGAGCCTCTTG (SEQ ID NO:39), NO:34)
- 25 20 PRO1378 has a calculated molecular weight of approximately 36,108 daltons and an estimated pt of 22, SEQ ID NO:33) is 335 amino acids long, with a signal peptide sequence at about amino acids 1-15. at nucleotide positions 2370 to 2372 (Figure 21; SEQ ID NO:32). The predicted polypeptide precursor (Figure an apparent translational initiation site at nucleotide positions 1365 to 1367 and ending at the stop codon found The full length DNA58730-1607 clone shown in Figure 21 comained a single open reading frame with

SP2_HUMAN, SHPSPRBB_1, SP23_HUMAN, P_W08158, and P_W08150. between the PRO1378 amino acid sequence and the following Dayhoff sequences: ICAL_RABIT. alignment analysis of the full-length sequence shown in Figure 22 (SEQ ID NO:33), revealed some homology An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

છ Clone DNAS8730-1607 was deposited with the ATCC on September 15, 1998, and is assigned ATCC

EXAMPLE 13: Isolation of CDNA clones Encoding Human PRO1481

35 human fetal kidney cDNA library that preferentially represents the 5' ends of the primary cDNA clones. Based of the full-length coding sequence for PRO1481 from a human fetal kidney cDNA library. on the DNA53254 sequence, oligonacicotides were symbesized for use as probes (or primers) to isolate a clone An initial DNA sequence, referred to herein as DNA53254, was identified using a yeast screen, in a

24. PRO1481 has a calculated molecular weight of approximately 36,294 daltons and an estimated pl of approximately 4.98. Clone DNA58732-1650 has been deposited with the ATCC and is assigned ATCC deposit domain is at about amino acids 235-262 of SEQ ID NO:41. The N-glycosylation sites are indicated in Figure SEQ ID NO:41) is 334 amino acids long. The signal peptide is at about amino acids 1-23, and a transmembrane nucleotide positions 1322-1324 (Figure 23: SEQ ID NO:40). The predicted polypeptide precursor (Figure 24, an appearent translational initiation site at nucleotide positions 320-322 and ending at the stop codon found at The full length DNA58732-1650 clone shown in Figure 23 contained a single open reading frame with

5 between the PRO1481 amino acid sequence and the following Dayhoff sequences (data incorporated herein): alignment analysis of the full-length sequence shown in Figure 24 (SEQ ID NO:41), revealed sequence identity YN23_YEAST, S67770, H36857, YLU2_PICAN, GEN12881, CVY15035_28, YM96_YEAST, ESC1_SCHPO CELZK783_1 and S59310. An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

EXAMPLE 16: Isolation of cDNA clones Encoding Human PRO1189

- 15 existing homologies. The homology search was performed using the computer program BLAST or BLAST? (LIFESEQTM, Incyte Pharmaceuticals, Palo Alto, CA; and Genentech, South San Francisco, CA) to identify databases which included public EST databases (e.g., GenBank) and proprietary EST DNA databases DNA41784. The DNA41784 sequence was then compared to a variety of expressed sequence tag (EST) A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated
- 20 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score Washington). The consensus sequence obtained therefrom is herein designated DNA45499. consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into
- 25 bone marrow library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRKSB (pRKSB is a precursor of pRKSD that does not contain the Sfil site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp. Based on the DNA45499 sequence, oligonucleotide probes were generated and used to screen a human

PCR primers (forward and reverse) were synthesized:

೪ forward PCR primer (45499.f2) 5'-GGGAACTGCTATCTGATGCC-3' (SEQ ID NO:45) TEVERSE PCR primer (45499:12) 5'-CACGATTCCCTCCACAGCAACTGGG-3' (SEQ ID NO:48). tevense PCR primet (45499.tl) 5°CTTCTCGAACCACATAAGTTTGAGGCAG-3' (SEQ ID NO:47) forward PCR primer (45499.f1) 5'-GAAAGACACGACACAGCAGCTTGC-3' (SEQ ID NO:44) forward PCR primer (45499-13) 5'-CAGGATCTCCTCTTGCAGTCTGCAGC-3' (SEQ ID NO:46)

sequence which had the following nucleotide sequence: Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45499

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hybridization probe (45499.p1)

5'-CGCCTTACCGCGCAGCCCGAAGATTCACTATGGTGAAAATCGCCTTCAAT-3' (SEQ ID NO:49)

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screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1189 gene using the probe oligonucleotide and one of the PCR primers. In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

(Figure 25; SEQ ID NO:42). The predicted polypeptide precursor is 263 amino acids long has a calculated at about amino acids 166-169. molecular weight of approximately 29,741 daltons and an estimated pl of approximately 5.74. Additional translational initiation site at nucleotide positions 79-81, and a stop signal at nucleotide positions 868-870 features include a type II transmembrane domain at about amino acids 53-75 and a potential N-glycosylation site A full length clone was identified that contained a single open reading frame with an apparent

5 alignment analysis of the full-length sequence shown in Figure 26 (SEQ ID NO:43), evidenced significant Dayhoff sequences: AF017985_1, CBRG01D9_2, 179662, and CHPDRBAG_1. Additionally, some homology was revealed between the PRO1189 amino acid sequence and the following homology between the PRO1189 amino acid sequence and Dayhoff sequences MUSE25A_1 and HS696H22_1. An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

Clone DNA58828-1519 has been deposited with ATCC and is assigned ATCC deposit no. 203172.

EXAMPLE 17: Isolation of cDNA clones Encoding Human PRO1415

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25 20 Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55720. BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and or BLAST2 (Altahul et al., Methods in Engrynology 266:460-480 (1996)). Those comparisons resulting in a CA) to identify existing homologies. The homology search was performed using the computer program BLAST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, sequence was then compared to a variety of expressed sequence ug (EST) databases which included public EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 150918. This EST cluster Use of the signal sequence algorithm described in Example 3 above allowed identification of m EST

within the Incyte EST clone no. 4081476, the Incyte EST clone no. 4081476 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 27 and is herein designated In light of the sequence homology between the DNA5S720 sequence and an EST sequence contained

ઝ 30 following: a signal peptide from about ammo acid 1 to about amino acid 25, a transmembrane domain from about site at nucleotide positions 148-150 and ending at the stop codon at nucleotide positions 997-999 (Figure 27) of the full-length PRO:415 sequence shown in Figure 28 (SEQ ID NO:50) evidences the presence of the amino acid 23, from about amino acid 40 to about amino acid 45, from about amino acid 46 to about amino acid amino acid 94 to about amino acid 118 and potential N-myristolation sites from about amino acid 18 to about shown in Figure 28 has an estimated molecular weight of about 29,191 daltons and a pl of about 4.52. Analysis The predicted polypeptide precursor is 283 amino acids long (Figure 28). The full-length PRO1415 protein Clone DNA58852-1637 contains a single open reading frame with an apparent translational initiation

51, from about amino acid 145 to about amino acid 150, from about amino acid 192 to about amino acid 197, from about amino acid 193 to about amino acid 216, from about amino acid 211 to about amino acid 216, from about amino acid 238 to about amino acid 242 and from about amino acid 242 to about amino acid 247. Close about amino acid 243 to about amino acid 247. Close DNA58832-1637 has been deposited with ATCC on September 22, 1998 and it assigned ATCC deposit no. 203271.

An analysis of the Dayboff database (vertion 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 28 (SEQ ID NO:50), evidenced significant bomology between the PRO1415 amino acid requence and the following Dayboff sequences: HSU66616_1, P_W24017, A38219, CD30_HUMAN, HSU78971_1, P_W22214, NFM_HUMAN, ADH1_ASPFL, PAU93274_5 and CENB_MOUSE.

EXAMPLE 18: Isolation of cDNA clones Encoding Human PRO1411.

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from an incyce database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ*, Incyce Pharmaccuticals, Palo Alto, CA) to identify existing bomologits. One or more of the ESTs were derived from a thryviol tissue library. The bomology search was performed using the computer program BLAST of BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those compartious resulting in a BLAST2 score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington). Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNAS6013.

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In light of the sequence homology between the DNA56013 acquence and an EST sequence contained within the Incyrte EST 1444225, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 29 and is herein designated as DNA59212-1627.

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The full length clone shown in Figure 29 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 184-186 and ending at the stop codon found at nucleotide positions 1504-1306 (Figure 29; SEQ ID NO:51). The predicted polypeptide precursor (Figure 39; SEQ ID NO:52) is 440 amino acids long. The signal peptide is at about amino acids 1-21, and the cell attachment site is at about amino acids 301-303 of SEQ ID NO:52. PRO1411 has a calculated molecular weight of approximately 42,208 dultons and an estimated pl of approximately 6.36. Clone DNA59212-1627 was deposited with the ATCC on September 9, 1998 and is assigned ATCC deposit no. 203245.

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An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST? sequence alignment analysis of the full-length sequence shown in Figure 30 (SEQ ID NO-52), revealed sequence identify between the PRO1411 amino acid sequence and the following Dayhoff sequences (data from database incorporated herein): MTV023_19, P_R05307, P_W26348, P_P82962, AF000949_1, EBN1_EBV, P_R95107, GRP2_PHAVU, P_R81318, and \$754439_1.

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EXAMPLE 19: Isolation of cDNA clones Encoding Human PRO1295

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., OenBank) and a proprietary EST DNA database (LIFESEQ®, lacyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One of more of the ESTs was derived from a thymus tissue library. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 256:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program 'phrap' (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein 10 designated DNA56262.

In light of the sequence homology between the DNA56262 sequence and an EST contained within the Incyce EST 3743334, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 31 and is berein designated as DNA59218-1559.

The full length clone shown in Figure 31 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 207-209 and ending at the stop codon found at nucleotide positions 1047-1049 (Figure 31; SEQ ID NO:53). The predicted polypeptide procursor (Figure 32, SEQ ID NO:54) is 280 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID NO:54. A targeting signal and N-glyocoylation site are also indicated in Figure 54. PRO1295 has a calculated molecular veight of approximately 30,163 dallons and an eximated 10 framewine with 6.7 Close New 2001 1670.

20 weight of approximately 30, 163 daltons and an estimated pl of approximately 6.87. Clone DNA59218-1559 was deposited with the ATCC on September 29, 1998 and is assigned ATCC deposit no. 203287.
An analysis of the Dayhoff database (version 35.45 SwissProx 35), using a WU-BLAST2 sequence

alignment analysis of the full-length sequence shown in Figure 32 (SEQ ID NO:54), revealed sequence identity between the PRO1295 amino acid sequence and the following Dayhoff sequences (data incorporated herein):

25 AB011099_1, ILVE_MYCTU, ATTECR_2, AF010496_27, P_R13346, S37191, PER_DROMS, L2MU_ADECC and P_W34238.

EXAMPLE 20: Isolation of cDNA clones Encoding Human PRO1359

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST of cluster sequence from an Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA databases (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a signoid colon tissue library. The homology search was performed using the computer program BIAST or BLAST2 (Altabut et al., Methods in Enzympology, 266:460-480 (1996)).

35 Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Scattle, Washington). The consensus sequence obtained therefrom is therein

esignated DNA56263.

In light of the sequence homology between the DNA-56263 sequence and the incyte EST 1931418, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Frigure 33 and is herein designated as DNA-59219-1613.

The full length clone shown in Figure 33 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 184-186 and ending at the stop codon found at nucleotide positions 1881-1883 (Figure 33, SEQ ID NO.55). The predicted polypopide precursor (Figure 34, SEQ ID NO.56) is 299 amino acids long. The transmembrane domain is at about amino acids 9-31 of SEQ ID NO.56. N-gylcosylation sites are at about amino acids 64-67 and 115-118 of SEQ ID NO.56. PRO1359 has a calculated molecular weight of approximately 34,291 daltons and an estimated pl of approximately 9.87. Clone

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10 DNAS9219-1613 was deposited with the ATCC on September 15, 1998 and is assigned ATCC deposit no. 203220.

An analysis of the Dayboff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 34 (SEQ ID NO.56), revealed sequence identity between the PRO1359 amino acid sequence and the following Dayboff sequences (data incorporated herein): GEM14384, P_R78622, A23699_1, P_R65244, A54898, AF059321_1, RNU55938_1, BTRNAST6_1, P_R75199 and P_R63216.

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EXAMPLE 21: Isolation of cDNA clones Encoding Human PRO1190

The method described in Example 1 above allowed the identification of a single Merck/Washington
20 University EST sequence, EST no. AA339802, which is designated herein as "DNA53943". Based on the
DNA53943 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that comtained
the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for
PRO1190.

PCR primers (forward and reverse) were synthesized:

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forward PCR primer: (33943.f1) GGAAACACAGCAGTCATTGCCTGC (SEQ ID NO:59)
reverse PCR primer: (33943.f1) GCACACGTAGCCTGTCGCTGGAGC (SEQ ID NO:60)
Additionally a combatic officeroplastic backets.

Additionally, a symbatic oligonucleoxide hybridization probe was constructed from the DNAS3943 sequence which had the following nucleoxide sequence:

hthidization probe: (53943.p1) CACCCCAAAGCCCAGGTCCGGTACAGCGTCAAACAAGAGTGG (SEQ

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In order to screen several libraries for a source of a full-length clome, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to toolate clones encoding the PRO1190 gene using the probe oligonucleotide and one of the PCR primers. RNA

35 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1190 (designated herein as DNA59586-1520 [Figure 35, SEQ ID NO:57]; and the derived protein sequence for PRO1190.

for construction of the cDNA libraries was isolated from human bone marrow.

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The entire coding sequence of PRO1190 is shown in Figure 35 (SEQ ID NO:57). Clone DNA59586-1520 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 340-342 and an apparent stop codon at nucleotide positions 3685-3687. The predicted polypoptide precursor is 1115 amino acids long. The full-length PRO1190 protein shown in Figure 36 has an estimated molecular weight of about 121,188 daltons and a pl of about 7.07. Other features of the PRO1190 protein include: two transmernbrane domains at amino acids 16-30 and 854-879; a cyrochrome P450 cystein heme-iron ligand signature at amino acids 1051-1060; an N-6 adenine-specific DNA methylases signature at amino acids 1051-1060; an N-6 adenine-specific DNA methylases signature at amino acids 1051-1060; and potential N-glycosylation sites at amino acids 65-68, 76-79, 98-101, 189-192, 275-278, 518-521, 726-729, and 760-763. Clone DNA59586-1520 was deposited with the ATCC on September 29, 1998, and is assigned ATCC deposit no. 202288.

An analysis of the Dayhoff database (version 33.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 36 (SEQ ID NO:58), revealed homology between the PRO1190 amino acid sequence and the following Dayhoff sequences: AP004840_1, AP004841_1, AF025465_1, HSU72391_1, P_R13144, AXO1_HUMAN, GEN13349, 158164, D87212_1, A53449, and D86983_1, and KIAA0230.

EXAMPLE 22: Isolation of cDNA clones Encoding Human PRO1772.

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A consensus DNA sequence was assembled relative to other EST sequences using plarap as described in Example I above. This consensus sequence is herein designated DNA45120. Based on the DNA45120 consensus sequence, oligonucleotides were symbosized: I) to identify by PCR a cDNA library that contained 20 the sequence of interest, and 2) for use as probes to isolate a close of the full-length coding sequence for PRO1772.

PCR primers (forward and reverse) were synthesized:

EXERTE PCR primer (45120.11) 5'-CCTTCACCTGCAGTACACCATGGGC.3' (SEQ ID NO:64)

INVESTMENT PCR primer (45120.11) 5'-GTCACACACAGGCTCTGGCAGCTGAG-3' (SEQ ID NO:65)

25 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45120 sequence which had the following nucleotide sequence

whridization probe (45120.pl)

S'-CCAAGTTCAGACACCACATGTACACCAACGTCAGCGGATTGACAAGC-3' (SEQ ID NO:66)
RNA for construction of the cDNA libraries was isolated from human bone marrow tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1772 (designated herein as DNA59817-1703 [Figure 37, SEQ ID NO:62]; and the derived protein sequence for PRO1772.

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The endre nucleatide sequence of DNA59817-1703 is shown in Figure 37 (SEQ ID NO:63). Clone DNA59817-1703 contains a single open reading frame with an apparent translational initiation site or nucleotide 35 positions 93-95 and ending at the stop codon at nucleotide positions 1554-1556 (Figure 37). The predicted polypophide precursor is 487 amino acids long (Figure 38). The full-length PRO1772 protein shown in Figure 38 has an estimated molecular weight of about 53,569 daltons and a pt of about 7.68. Analysis of the full-length

from about amino acid 472 to about amino acid 477 and a prokazyotic membrane lipoprotein lipid attachment to about amino acid 46, from about amino acid 59 to about amino acid 64, from about amino acid 73 to about 329, from about amino acid 354 to about amino acid 359, from about amino acid 357 to about amino acid 362, on November 17, 1998 and is assigned ATCC deposit no. 203470. site from about amino acid 136 to about amino acid 146. Clone DNAS9817-1703 has been deposited with ATCC from about amino acid 394 to about amino acid 399, from about amino acid 427 to about amino acid 432 and acid 187, from about amino acid 194 to about amino acid 199, from about amino acid 324 to about amino acid amino acid 78, from about amino acid 133 to about amino acid 138, from about amino acid 182 to about amino from about amino acid 333 to about amino acid 336, potential N-myristolation sites from about amino acid 41 from about amino ocid 184 to about amino acid 187, from about amino acid 243 to about amino ocid 246 and to about amino acid 331, potential N-glycosylation sites from about amino acid 119 to about amino acid 122, peptide from ahout amino acid 1 to about amino acid 36, a transmembrane domain from about amino acid 313 PRO1772 sequence shown in Figure 38 (SEQ ID NO:63) evidences the presence of the following: a signal

homology between the PRO1772 amino acid sequence and the following Dayhoff sequences: P_R30823, MDPI_PIG, MDPI_HUMAN, P_R13857, P_RS3920, MDPI_MOUSE, P_R30822, JC4222, CELF52C6_2 alignment analysis of the full-length sequence shown in Figure 38 (SEQ ID NO:63), evidenced significant An analysis of the Dayhoff database (version 33.45 SwissProt 35), using a WU-BLAST2 sequence

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EXAMPLE 23: Isolation of cDNA clones Encoding Human PRO1248

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or BLAST2 (Altahul et al., Methods in Eurymology 266.460-480 (1996)). Those comparisons resulting in a Seaule, Washington). The consensus sequence obtained therefrom is herein designated DNAS6056 BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and CA) to identify existing homologies. The homology search was performed using the computer program BLAST cluster sequence from the Incyre database, designated Incyte EST cluster sequence no. 7494. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

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- 30 Merrk EST clone no. AA404441, the Merrk EST clone no. AA404441 was purchased and the cDNA insert was DNA60278-1530. obtained and sequenced. The sequence of this cDNA insert is shown in Figure 39 and is herein designated as In light of the sequence homology between the DNAS6056 sequence and an EST contained within the
- 35 The predicted polypeptide preversor is 183 amino acids long (Figure 40). The full-length PRO1248 protein Clone DNA60278-1530 contains a single open reading frame with an apparent translational initiation

of the full-length PRO1248 sequence shown in Figure 40 (SEQ ID NO:68) evidences the presence of the shown in Figure 40 has an estimated molecular weight of about 20,574 daltons and a pl of about 6.60. Analysis site at nucleotide positions 122-124 and ending at the stop codon at nucleotide positions 671-673 (Figure 39).

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acid 50. Clone DNA60278-1530 has been deposited with ATCC on September 1, 1998 and is assigned ATCC amino acid 90 to about amino acid 112 and potential N-glycosylation sites from about amino acid 21 to about following: a signal peptide from about amino acid 1 to about amino acid 20, a transmembrane domain from about amino scid 24, from sbout amino acid 38 to about amino acid 41 and from about amino acid 47 to about amino

homology between the PRO1248 amino acid sequence and the following Dayhoff sequences: AF026198_5 CELR12C12_5, PN0563, S64541_1, PN0564, P_R44881 and XLU78189_1. alignment analysis of the full-length sequence shown in Figure 40 (SEQ ID NO:68), evidenced significant An analysis of the Dayboff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

EXAMPLE 24: Isolation of cDNA clones Encoding Human PRO1316

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BLAST or BLAST2 [Altschul et al., Methods in Enzymology 266: 460-480 (1996)] as a comparison of the ECD databases known to comtain secreted sequences were used to search various publicly available EST (Expressed Sequenced Tag) databases (GenBank, Merck/Wash. U). The search was performed using the computer program The extracellular domain (ECD) which includes the signal sequence, if any, of publicly available

15 into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, WA) of 70 (or in some cases 90) or greater that did not did not encode known proteins were clustered and assembled protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score The above search resulted in the identification of the EST, designated W55979 which showed homology

20 from Mcrck/Washington University and the cDNA insert was obtained and sequenced in its entirety. with the secreted protein Dkk-1. The clone corresponding to EST W55979 (clone NbHH19W) was purchased

ዩ (211-283), an N-glycosylation site (364-366), and the Zn(2)-Cys(6) binuclear cluster domain (505-655). Clone acids long. Additional regions of significant interest include the nucleotide residues encoding the signal peptide at nucleotide positions 988-990 (Figure 42: SEQ ID NO:70). The predicted polypeptide precursor is 259 amino PRO1316 protein shown in Figure 42 has an eximated molecular weight of about 28,447 daltons and a pl of DNA60608-1577 has been deposited with ATCC and is assigned ATCC deposit no. 203126. The full-length open reading frame with an apparent translational initiation site at nucleotide positions 211-213, and a stop codor encoded by the purchased clone, is shown in Figure 41 (SEQ ID NO:69). DNA60608-1577 contains a single The nucleic acid sequence corresponding to the full length PRO1316 (designated DNA60608-1577)

30 the full-length sequence, PRO1316 shows significant amino acid sequence identity to the dicktopf family of YQ16_CAEEL. ITB6_HUMAN, CONO_LYMST, S41033, D63483_1, D86864_1 and AB001978_1 proteins. Additionally, DNA60608 has shown homology to AF030433_1, LFE4_CHICK, COL_RABIT, Based on a BLAST and FastA sequence alignment analysis (using the ALIGN computer program) of

35 EXAMPLE 25: Isolation of cDNA clores Encoding Human PRO1197

buman SK-Lu-1 adenocarcinoma cDNA library that preferentially represents the 5' ends of the primary cDNA An initial DNA sequence, referred to herein as DNA56267, was identified using a yeast screen, in a

clones. DNA56267 was used to synthesize oligonoucleotides for use as probes to isolate a clone of the full-length coding sequence for PRO1197 from a human breast carcinoma cDNA library.

SEQ ID NO:73: 5'AATTCATGGCAAATATTTCCCTTCCC3' (forward);

SEQ ID NO:74: 5'TGGTAAACTGGCCCAAACTCGG3' (reverse); and

The full length DNA60611-1524 clone shown in Figure 43 contained a single open reading frame with an apparent translational initiation site at mucleotide positions 311-313 zull ending at the stop codon found at nucleotide positions 1400-1402 (Figure 43; SEQ ID NO.71). The predicted polypeptide precursor (Figure 44, SEQ ID NO.72) is 363 amino acids long. The signal peptide is at about amino acids 1-24 of SEQ ID NO.72.

10 PRO1197 has a calculated molecular weight of approximately 38.825 dations and an estimated pf of approximately 9.88. Clone DNA60611-1524 has been deposited with ATCC and is assigned ATCC deposit no. 203175.

An analysis of the Dayhoff dambase (version 35.45 SwissProt 35), using a WU-BLASTZ sequence alignment analysis of the full-length sequence shown in Figure 44 (SEQ ID NO:72), revealed sequence identify between the PRO1197 amino acid sequence and the following Dayhoff sequences (information from database incorporated herein): Y144_HUMAN, 147141 (a gastric mucin, mucins are described in Ann.NY Acad. Sci., 140(2):804-834 (1967), AMYH_YEAST, CELK/06A9_3, CELZK/783_1, HKR1_YEAST, AB003521_1, D87895_1, S61993 and YM96_YEAST.

20 EXAMPLE 26: Isolation of cDNA clones Encoding Human PRO1293.

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 113204. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq*, Incyte Pharmaceuticals, Palo Alto CA) to identify existing bornologies. The homology search was performed using the communication of the continuous properties.

- 25 CA) to identify existing bornologies. The hornology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in <u>Enzymology 266</u>:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is berein designated DNA56522.
- 30 In light of the sequence hormology between the DNAS6522 sequence and an EST contained within the Incyre EST clone no. 2966119, the Incyre EST clone no. 2966119 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 45 and is berein designated as DNAS6618.1557.

Clone DNA60618-1557 contains a single open reading frame with an apparent translational initiation 35 site at nucleotide positions 37-39 and entiting at the stop codon at nucleotide positions (1060-1062 (Figure 45). The predicted polypeptide precursor is 341 amino acids long (Figure 46). The full-length PRO1293 protein shown in Figure 46 has an estimated molecular weight of about 38,070 daltons and a p1 of about 6.88. Analysis

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of the full-length PRO1293 sequence shown in Figure 46 (SEQ ID NO.77) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transmembrane domain from about amino acid 237 to about amino acid 262, a potential N-glycosylation site from about amino acid 205 to about amino acid 208, a cell attachment sequence from about amino acid 151 to about amino acid 152 and an amino acid sequence block having homology to copropophyrinogen III oxidase proteins from about amino acid 140. Clone DNA60618-1557 has been deposited with ATCC on September 29, 1998 and

An analysis of the Dayhoff database (version 35.45 Swissbrot 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 46 (SEQ ID NO:77), evidenced significant homology between the PRO1293 amino acid sequence and the following Dayhoff sequences: HSVCD54_1,

is assigned ATCC deposit no. 203292.

A33_HUMAN, AF009220_1, HSU82279_1, AF004230_1, P_R13272, AF004231_1, AF043644_1, S44125 and IISIGGHC85_1.

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EXAMPLE 27: Isolation of cDNA clones Encoding Human PRO1380

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated

15 DNA45776. Based on the DNA45776 sequence, oligonucleotide probes were generated and used to screen a
human retina library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRKSB

(pRKSB is a precursor of pRK5D that does not contain the Sfil site; see, Holmes et al., Science, 252:1278-1280

(1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

- 20 forward PCR primer (45776.01). 5' TITTGCGGTCACCATTGTCTGC.3' (SEQ ID NO:80) and reverse PCR primer (45776.11). 5' CGTAGGTGACACAGAAGCCCAGG.3' (SEQ ID NO:81). Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45776 sequence which had the following nucleotide sequence: http://doi.org/10.1001
- 25 5-TACGGCATGACCGGCTCCTTTCCTATGAGGAACTCCCCAGGCACTGATAT-3' (SEQ ID NO:82).

 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

In order to screen several libraries for a source of a full-length close, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to itolate closes encoding the PRO1380 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent of translational initiation size at nucleotide positions 36-38, and a stop signal at nucleotide positions 1461-1463 (Figure 47; SEQ ID NO:78). The predicted polypeptide precursor is 470 amino acids long has a calculated molecular weight of approximately 51,715 daltons and an estimated pl of approximately 7.86. Additional features include transmembrane domains at about amino acids 50-74, 105-127, 135-133, 163-183, 228-222, 305-330, and 448-472; potential N-glycosylation sizes at about amino acids 14-17 and 84-87; and a dihydrofolate 35 reductase alignature at about amino acids 60-68.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 48 (SEQ ID NO:79), evidenced homology

CEK02E11_1, AF034102_1, JC4196, CEF36H2_2, P_R92315, YAC2_YEAST, F1707_13, and CEF44D12_3. between the PRO1380 amino acid sequence and the following Dayhoff sequences: HSU81375_1, CEZK809_6. Clone DNA60740-1615 was deposited with the ATCC on November 3, 1998, and is assigned ATCC

S EXAMPLE 28: Isolation of cDNA clones Encoding Human PRO1265

from RNA isolated from inflamed human adenoid tissue. The consensus sequence obtained therefrom is herein identify existing homologies. The bomology search was performed using the computer program BLAST or Seaule, Washington). One or more of the ESTs used in the assembly was derived from a cDNA library prepared assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and BLAST2 (Altshul et al., Methods in Enzymology, 266:460-480 (1996)). Those comparisons resulting in a (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ*, Incyre Pharmaceuticals, Palo Alto, CA) to cluster sequence from the LIFESEQ* database, designated EST Cluster No. 86995. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases Use of the signal sequence algorithm described in Example 3 above allowed identification of an ES?

sequenced. The sequence of this cDNA insert is shown in Figure 49 and is herein designated as DNA60764 within Incyte EST no. 20965, EST clone no. 20965 was purchased and the cDNA insert was obtained and In light of the sequence homology between the DNASS717 sequence and an EST sequence contained

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1-21; potential N-glycosylation sites at about amino acids 54-57, 134-137, 220-223, and 559-562; and a region having amino acid sequence identity with D-amino acid oxidase proteins at about amino acids 61-80. 567 amino acids long. PRO1265 has a calculated molecular weight of approximately 62,881 daltons and an 1780-1782 (Figure 49; SEQ ID NO:83). The predicted polypeptide procursor (Figure 50, SEQ ID NO:84) is estimated pl of approximately 8.97. Additional features include a signal peptide sequence at about amino acids translational initiation site at nucleotide positions 79-81 and ending at the stop codon found at nucleotide positions The full length clone shown in Figure 49 contained a single open reading frame with an apparent

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Sequence homology was also found to exist between the full-length sequence shown in Figure 50 (SEQ ID NO:84) and the following additional Dayhoff sequences: BC542A_1, E69899, S76290, MTV014_14, AOFB_HUMAN, ZMJ002204_1, S45812_1, DBRNAPD_1, and CRT1_SOYBN equence identity between the PRO1265 amino acid sequence and Dayhoff sequence no. MMU70429_1. alignment analysis of the full-length sequence shown in Figure 50 (SEQ ID NO:84), revealed significant An analysis of the Dayhoff database (version 35.45 SwitsProt 35), using a WU-BLAST2 sequence

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Clone DNA60764-1533 was deposited with the ATCC on November 10, 1998, and is assigned ATCC

EXAMPLE 29: Isolation of cDNA clones Encoding Human PRO1250

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

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or BLAST2 (Altahul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a CA) to identify existing homologies. The homology search was performed using the computer program BLAST databases (e.g., GenBank) and a proprietury EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto sequence was then compared to a variety of expressed sequence 12g (EST) databases which included public EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 56523. This EST cluster

BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and Seartle, Washington). The consensus sequence obtained therefrom is berein designated DNA56103. assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, In light of the sequence homology between the DNA56103 sequence and an EST sequence contained

was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 51 and is herein designated within the Incyce EST clone no. 3371784, the Incyce EST clone no. 3371784 was purchased and the cDNA insert

The predicted polypeptide precursor is 739 amino acids long (Figure 52). The full-length PRO1250 protein site at nucleotide positions 74-76 and ending at the stop codon at nucleotide positions 2291-2293 (Figure 51) Clone DNA60775-1532 contains a single open reading frame with an apparent translational initiation

20 shown in Figure 52 has an estimated molecular weight of about 82,263 daltons and a pl of about 7.55. Analysis amino avid 591 and from about amino acid 619 to about amino acid 622. Clone DNA60775-1532 has been deposited with ATCC on September 1, 1998 and is assigned ATCC deposit no. 203173. glycosylation sites from about amino acid 102 to about amino acid 105, from about amino acid 588 to about following: a type II transmembrane domain from about amino acid 61 to about amino acid 80, a putative AMP. of the full-length PRO1250 sequence shown in Figure 52 (SEQ ID NO:86) evidences the presence of the binding domain signature sequence from about amino acid 314 to about amino acid 325, and potential N

ઇ \$56508_1, BNAMPBP2_1, BNACS7_1, CELT08B1_6, CELC46F4_2, AF008206_6, CELR07C3_11 alignment analysis of the full-length sequence shown in Figure 52 (SEQ ID NO:86), evidenced significant LMU70253_2 and AF008206_7. homology between the PRO1230 amino acid sequence and the following Dayhoff sequences: LCFB_HUMAN An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

EXAMPLE 30: Isolation of cDNA clones Encoding Human PRO1475

30 in Example 1 above. This convensus sequence is herein designated DNA45639. Based on the DNA45639 the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for consensus sequence, oligoracieotides were synthesized: 1) to identify by PCR a cDNA library that contained A consensus DNA sequence was assumbled relative to other EST sequences using phrap as described

PCR primers (forward and reverse) were synthesized:

33 forward PCR primer (45639.f1) 5'-GATGGCAAAACGTGTGTTTTGACACG-3' (SEQ ID NO:89) reverse PCR primer (45639.r1) ODWard PCR primer (45639.72) S'-CCCAGGCAGAGATGCAGTACAGGC-3' (SEQ ID NO:91) 5'-CCTCAACCAGGCCACGGGCCAC-3' (SEQ ID NO:90)

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hybridization probe (45639.p1) sequence which had the following nucleotide sequence Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45639 (SEQ ID NO:92)

5'-CTCACCTCATGAGGATGAGGCCATGGTGCTATTCCTCAACATGGTAG-3' (SEQ ID NO:93)

screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to for construction of the cDNA libraries was isolated from human fetal brain tissue isolate clones encoding the PRO1475 gene using the probe oligonucleoride and one of the PCR primers. RNA In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

10 PRO1473 (designated herein as DNA61185-1646 [Figure 53, SEQ ID NO:87]; and the derived protein sequence DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

20 ᅜ ATCC on November 17, 1998 and is assigned ATCC deposit no. 203464. 54 has an estimated molecular weight of about 75,220 daltons and a pl of about 6.76. Analysis of the full-length polypeptide precursor is 660 amino acids long (Figure 54). The full-length PRO1475 protein shown in Figure PRO1475 sequence shown in Figure 54 (SEQ ID NO:88) evidences the presence of the following: a DNA61185-1646 contains a single open reading frame with an apparent translational initiation site at mucleotide GNT1 from about amino acid 229 to about amino acid 660. Clone DNA61185-1646 has been deposited with transmembrane domain from about amino acid 38 to about amino acid 55 and a homologous region to mouse positions 130-132 and ending at the stop codon at nucleotide positions 2110-2112 (Figure 53). The predicted The entire nucleotide sequence of DNA61185-1646 is shown in Figure 53 (SEQ ID NO:87). Clone

219_HUMAN and EF07_MOUSE CGU65792_1, CGU65791_1, P_R24781, CELF48E3_1, G786_HUMAN, P_W06547, GNT1_CAEEL, homology between the PRO1475 amino acid sequence and the following Dayhoff sequences: GNT1_MOUSE, alignment analysis of the full-length sequence shown in Figure 54 (SEQ ID NO:88), evidenced significant An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

EXAMPLE 31: Isolation of cDNA clones Encoding Human PRO1377.

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30 cDNA clones. Based on the DNA46892 sequence, the following oligonucleotides were synthesized for use as (SEQID NO:97), and GGATGATTTCATCTCCATTAGCCTGTGTCTCTGGCTATGTTGGTGGGAT(SEQ probes to isolate a cione of the full-length coding sequence for PRO1377 from a human fetal kidney cDNA human umbilical vein endothelial cell cDNA library that preferentially represents the 5' ends of the primary library: GTTGTGGGTGAATAAAGGAGGGCAG (SEQ ID NO:96), CTGTGCTCATGTTCATGGACAACTG An initial DNA sequence, referred to herein as DNA46892, was identified using a yeast screen, in a

35 nucleoride positions 1070-1072 (Figure 55; SEQ ID NO:94). The predicted polypeptide precursor (Figure 56, an apparent translational initiation site at nucleotide positions 149-151 and ending at the stop codon found at The full length DNA61608-1606 clone shown in Figure 55 contained a single open reading frame with

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daltons and an estimated pl of approximately 6.52. Additional features include: a signal peptide at about amino SEQ ID NO:95) is 307 amino acids long. PRO 1377 has a calculated molecular weight of approximately 32,251 at about amino acids 37-56, 106-122, 211-230, 240-260, and 288-304 acids 1-18; potential N-glycosylation sites at about amino acids 29-32 and 241-244, and transmembrane domains

aligrament analysis of the full-length sequence shown in Figure 56 (SEQ ID NO:95), revealed some homology CEF26D10_3, \$66962, ATX2_YEAST, CEH13N06_8, \$49959, YIC3_YEAST, G02273, and P_W35557. between the PRO1377 amino acid sequence and the following Dayhoff sequences: CET01D3_6, CET28F3_4, Clone DNA61608-1606 has been deposited with ATCC and is assigned ATCC deposit no. 203239 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

5 EXAMPLE 32: Isulation of cDNA clones Encoding Human PRO1326

databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database "DNA 10295". This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) cluster sequence from the LIFESEQ® database, designated Incyte Cluster No. 59366, also referred herein as Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

20 15 (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was 480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not isolated from tumor tixtue removed from the penis of a male with squamous cell carcinoms. The consensus (Phil Green, University of Washington, Seartle, Washington). One or more of the ESTs was derived from RNA encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Euzynnology, 266:460

25 sequenced in its entirety. The sequence of this cDNA insert is shown in Figure 57 and is herein designated as within Incyte EST no. 1450878, the EST clone 1450878 was purchased and the cDNA insert was obtained and In light of the sequence homology between the DNAS6257 sequence and an EST sequence contained

sequence obtained therefrom is herein designated DNAS6257

The full length clone shown in Figure 57 contained a single open reading frame with an apparen

30 amino acids 1-29; a ribosomal protein S3Ae homologous region at about amino acids 129-166; and potential deposited with the ATCC on October 20, 1998 and is assigned ATCC deposit no. 203358. weight of approximately 45,333 daltons and an estimated pl of approximately 4.95. Clone DNA62808-1582 was N-glycosylation sites at about amino acids 109-112, 144-147 and 398-401. PRO1326 has a calculated molecular NO:100) is 401 amino acids long. Other features of the PRO1326 protein include: a signal sequence at about positions 1315 to 1317 (Figure 57; SEQ ID NO:99). The predicted polypeptide precursor (Figure 58, SEQ ID translational initiation site at nucleotide positions 112 to 114 and ending at the stop codon found at nucleotide

35 alignment analysis of the full-length sequence shown in Figure 58 (SEQ ID NO:100), revealed some homology HROMHCEMB_1,CEF47A4_2,A4S592,MYSP_HUMAN,NFU43192_1,ONGMBWMZ_1,CELC25A11_2, between the PRO1326 amino acid sequence and the following Dayhoff sequences: AC004013_1 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

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CELC25A11_1, and A42184

EXAMPLE 33: Isolation of cDNA clones Encoding Human PRO1249

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ascembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56060 BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and BLASTZ (Allahul et al., Methods in Enzymplogy, 266:460-480 (1996)). Those comparisons resulting in a identify existing homologies. The homology search was performed using the computer program BLAST or (c.g., GenBank) and a proprietary EST DNA database (Lifeseq®, incyte Pharmaceuticals, Palo Alto, CA) to was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases cluster sequence from the Incyte database, designated Incyte EST cluster no. 122605. This EST cluster sequence Use of the signal sequence algorithm described in Example 3 above allowed identification of an ES7

was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 59 and is herein designated within the Incyre EST clone no. 2630770, the Incyre EST clone no. 2630770 was purchased and the cDNA insert In light of the sequence homology between the DNA56060 sequence and an EST sequence contained

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555, from about amino acid position 831 to about amino acid position 850, from about amino acid position 1016 the full-length PRO1249 sequence shown in Figure 60 (SEQ ID NO:102) evidences the presence of the ATCC deposit no. 203237. a lencine zipper pattern sequence from about amino acid 843 to about amino acid 864 and potential Nto about amino acid position 1034 and from about amino acid position 1052 to about amino acid position 1070, predicted polypeptide precursor is 1089 amino acids long (Figure 60). The full-length PRO1249 protein shown glycosylations sites from about amino acid 37 to about amino acid 40 and from about amino acid 268 to about position 510 to about amino acid position 527, from about amino acid position 538 to about amino acid position acid position 470, from about amino acid position 481 to about amino acid position 500, from about amino acid site at nucleotide positions 3.5 and ending at the stop codon at nucleotide positions 3270-3272 (Figure 59). The amino acid 271. Clone DNA62809-1531 has been deposited with ATCC on September 9, 1998 and is assigned amino acid position 317 to about amino acid position 341, from about amino acid position 451 to about amino following: a signal peptide from about amino acid 1 to about amino acid 16, transmembrane domains from about in Figure 60 has an estimated molecular weight of about 118,699 daltons and a pl of about 8.49. Analysis of Clone DNA62809-1531 comains a single open reading frame with an apparent translational initiation

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and AF060218_4. AB004539_7, S64782, S62432, YJG2_YEAST, CELC27A12_8, YKQ5_YEAST, AB009505_3, SPBC24E9_8 homology between the PRO1249 amino acid sequence and the following Dayhoff sequences: AC004472_3, alignment analysis of the full-length sequence shown in Figure 60 (SEQ ID NO:102), evidenced significant An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLASTZ sequence

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EXAMPLE 34: Isolation of cDNA clones Encoding Human PRO1315

the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for in Example 1 above. This consensus sequence is herein designated DNA35925. Based on the DNA35925 consensus sequence, oligonucleosides were synthesized: 1) to identify by PCR a cDNA library that contained A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

PCR primers (forward and reverse) were synthesized:

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forward PCR primer (35925.f1) 5' CGCTGCTGCTGCTGCTCCTGU-3' (SEQ ID NO:105) forward PCR primer (35925,f2) S'-CAGTGTGCCAGGACTTTG-3' (SEQ ID NO: 106)

forward PCR primer (35925.f3) 5'-AGTCGCAGGCAGCGTTGG-3' (SEQ ID NO:107)

5 REVERSE PCR printed (33925.11). 5'-CTCCTCCGAGTCTGTGTGCTGCTGC:3' (SEQ ID NO:108) Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35925 hybridization probe (35925.01) sequence which had the following nucleotide sequence

15 5'-GGACGGGCAGTTCCCTGTGTCTCTGGTGGTTTGCCTAAACCTGCAAACATC-3' (SEQ ID NO:109) in order to screen several libraries for a source of a full-length clone, DNA from the libraries was

screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to for construction of the cDNA libraries was isolated from human retina tissue. isolate clanes encoding the PRO1315 gene using the probe oligonucleotide and one of the PCR primers. RNA

20 PRO1315 (designated herein as DNA62815-1576 [Figure 61, SEQ ID NO:103]; and the derived protein sequence for PRO1315. DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

ઇ polypeptide precursor is 442 amino acids long (Figure 62). The full-tength PRO1315 protein shown in Figure to about amino acid 163 and potential N-glycosylation sites from about amino acid 71 to about amino acid 74 PRO1315 sequence shown in Figure 62 (SEQ ID NO:104) evidences the presence of the following: a signal 62 has an estimated molecular weight of about 49,932 dattons and a pl of about 4.55. Analysis of the full-length peptide from about amino acid 1 to about amino acid 28, a transmembrane domain from about amino acid 140 positions 121-123 and ending at the stop codon at nucleotide positions 1447-1449 (Figure 61). The predicted DNA62815-1576 contains a single open reading frame with an apparent translational initiation site at nucleotide The entire nucleotide sequence of DNA62815-1576 is shown in Figure 61 (SEQ ID NO:103). Clore

30 from about amino acid 80 to about amino acid 83, from about amino acid 89 to about amino acid 92, from about DNA62815-1576 has been deposited with ATCC on September 9, 1998 and is assigned ATCC deposit no. amino acid 204 to about amino acid 207 and from about amino acid 423 to about amino acid 426. Clone

ß alignment analysis of the full-length sequence shown in Figure 62 (SEQ ID NO:104), evidenced significant NYYD8571_2, B64560, STMSLPE_1, P_R80508, P_W19258, A55817, GEN14043, AE000768_7 and homology between the PRO1315 amino acid sequence and the following Dayhoff sequences: MMU53696_1, An analysis of the Dayboff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

RNMUCASGPS_tpSMC.

EXAMPLE 35: Isolation of cDNA clones Encoding Human PRO1599

Incyte EST no. 1491360 was identified as a sequence of interest using the techniques described in Example I above having a BLAST score of 70 or greater that does not encode a known protein. The nucleotide sequence of EST no. 1491360 and its complementary sequence is designated herein 'DNA37192'. Based on the DNA37192 sequence, oligomucleotides were synthesized: I) to identify by PCR a cDNA ilbrary that contained the sequence of interest, and 2) for use as probes to isolate a cloure of the full-length coding sequence for PRO1400

PCR primers (forward and reverse) were synthesized:

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[STWARD PCR DELECT CACGACAGCACCCCTGGAAG (37192.11; SEQ ID NO:112)
TEVETSE PCR DELECT CAGAAAGGAAACGAGGCCCGTGAG (37192.11; SEQ ID NO:113)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the contensus DNA37192 sequence which had the following nucleotide sequence:

<u>hybridization_probe</u>: TGACACTTACCATGCTCTGCACCCGCAGTGGGGACAGCCACAGA (SEQ ID 15 NO:114).

In order to streen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1599 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue.

20 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1599 (designated herein as DNA62845-1684 [Figure 63, SEQ ID NO:110]; and the derived protein sequence for PRO1599.

The entire coding sequence of PRO1599 is shown in Figure 63 (SEQ ID NO:110). Clone DNA628451684 contains a single open reading frame with an apparent translational initiation site at nucleotide positions
69-71 and an apparent stop coden at nucleotide positions 918-920. The predicted polypeptide procursor is 283
amino acids long. The full-length PRO1599 protein shown in Figure 64 has an estimated molecular weight of
about 30,350 daltons and a pl of about 9.66. Additional features of PRO1599 include: a signal peptide at about
amino acids 1-30; potential N-glycoxylation sites at about amino acids 129-132 and 189-192; a potential eAMP
and cGMP-dependent protein kinese phosphorylation site at about amino acids 263-266; potential Nmyristoylation sites at about amino acids 28-33, 55-60, 174-179, and 236-241; a potential amidation site at about
myristoylation sites at about amino acids 28-30.

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An analysis of the Dayhoff database (version 35.45 SwitsProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 64 (SEQ ID NO:111), revealed significant homology between the PRO1599 amino acid sequence and the following Dayhoff sequence: CFAD_PIG. Homology was also found between the PRO1599 amino acids sequence and the following additional Dayhoff sequences. CFAD_HUMAN:P_R05421:P_R55757;P_R05772;GRAM_HUMAN: MUSLMET_1: P_P80335;P_RS5758; A42048_1; and P_W05383.

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Clone DNA62845-1684 was deposited with the ATCC on October 20, 1998 and is assigned ATCC

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EXAMPLE 36: Isolation of cDNA clones Encoding Human PRO1430

deposit no. 203361.

A DNA sequence designated herein as DNA49433 was obtained as described in Example 1 above.

Merck EST no. T49469, which was identified as being an EST of interest from the assembly, was purchased and the cDNA insert was obtained and sequenced in entirety.

DNA sequencing of the clone as described above gave the full-length DNA sequence for PRO1430, which is designated herein as "DNA64842-1632" (SEQ ID NO:115), and the derived protein sequence for PRO1430 (SEQ ID NO:116). Clone DNA64842-1632 comtains a single open reading frame with an apparent translational initiation site at mucleotide positions 82-84, and an apparent stop condon at nucleotide positions 1075-

10 translational initiation site at nucleotide positions 82,84, and an apparent stop codon at nucleotide positions 1075.
1077. The full-length PRO1430 protein shown in Figure 66 has an estimated molecular weight of about 35,932 dattons and a pl of about 8.45. The predicted polypeptide precursor is 331 amino acids long. Additional features include a signal peptide at about amino acids 1-17; a potential N-glycosylation site at about amino acids 171-174, and regions of homology with short chain alcohol dehydrogenase family proteins at about amino acids 29.51, 116-126, 180-217, and 222-230.

An analysis of the Dayhoff database (version 33.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 66 (SEQ ID NO:116), revealed significant homology between the PRO1430 amino acid sequence and Dayhoff sequence no. P_W03198. Homology was also found between the PRO1430 amino acid sequence and the following Dayhoff sequences: MTV030_10.

20 MTV037_2, A40116_1, S42651, CEC15H11_6, SPCC736_13, SCU43704_1, S19842, OXIR_STRAT, and OXIR_STRAL.

Clone DNA64842-1632 has been deposited with ATCC and is assigned ATCC deposit no. 203278.

EXAMPLE 37: Isolation of cDNA clones Encoding Human PRO1374

A consensus DNA sequence encoding PRO1374 was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein *DNA47357". Based on the DNA47357 convensus sequence, oligonucleoxides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1374.

PCR primers (forward and reverse) were synthesized:

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forward PCR primer 5' CGGGACAGGAGACCCAGAAAGGG3' (SEQ ID NO:119) and reverse PCR primer 5' GGCCAAGTGATCCAAGGCATCTTC3' (SEQ ID NO:120).

Additionally, a synthetic oligonucleotide bybridization probe was constructed from the consensus DNA47357 sequence which had the following nucleotide sequence:

ID NO:121).

In order to screen several libraries for a source of a full-length clone. DNA from the libraries was

isolate clones encoding the PRO1374 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from a human adenocarcinoma cell line. screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to

PRO1374 and the derived protein sequence for PRO1374. DNA sequencing of the closes isolated as described above gave the full-length DNA sequence for

Clone DNA64849-1604 has been deposited with the ATCC and is assigned ATCC deposit no. 203468. The fulllength PRO1374 protein shown in Figure 68 has an estimated molecular weight of about 61,126 daltons and sites, leucine zipper patterns, and ribonucleotide reductase small subunit signature are indicated in Figure 68 polypeptide precursor is 544 amino acids long. The approximate locations of the signal peptide, N-glycosylation 20-22 and an apparent stop codon at mulerotitle positions 1633-1655 of SEQ ID NO:117. The predicted 1604 contains a single open reading frame with an apparent translational initiation site at nucleotide positions The entire coding sequence of PRO1374 is shown in Figure 67 (SEQ ID NO:117). Clone DNA64849.

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\$44204, CET28D6_1, CET20B3_6, CELC14E2_3, CUAL_CHICK, ATM712_3, \$74997 and HIVH5994R8_1. between the PRO1374 amino acid sequence and the following Dayhoff sequences: CEF35G2_4, P_W37046 alignment analysis of the full-length sequence shown in Figure 68 (SEQID NO:118), revealed sequence identity An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

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EXAMPLE 38: Isolation of cDNA clones Encoding Human PRO1311

- ೪ 23 20 that does not comain the Sfil site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size ou was less than 2800 bp. oligonuclemide probes were generated and used to screen a human aortic endothelial cell library prepared as DNA sequences with the program "phrap" (Phil Green, University of Washington, Seartle, Washington). The in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus ct al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or (LIFESEQ , Incyte Pharmaceuticals, Palo Alto, CA; Genentech, South San Franscisco, CA) to identify existing DNA37721. The DNA37721 sequence was then compared to a variety of expressed sequence tag (EST) described in paragraph 1 of Example 2 above. The cloning vector was pRKSB (pRKSB is a precursor of pRKSD consensus sequence obtained therefrom is herein designated "DNA48616". Based on the DNA48616 sequence, bomologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul databases which included public EST databases (e.g., GenBank) and proprietary EST DNA databases A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated
- PCR primers (forward and reverse) were synthesized:
- reverse PCR primer (48616,r1) 5'-GACAGAGTGCTCCATGATGATGTCC-3' (SEQ ID NO:125) Sorward PCR_primer (48616.f1) 5'-ATCATCTATTCCACCGTGTTCTGGC-3' (SEQ ID NO: 124)
- which had the following nucleotide sequence: Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA48616 sequence

35 hybridization probe (48616.p1)

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screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to 5'-CCTGTCTGTGGGCATCTATGCAGAGGTTGAGCGGCAGAAATATAAAACCC-3' (SEQ ID NO:126) isolate clones encoding the PRO1311 gene using the probe oligonucleotide and one of the PCR princers. in order to screen several libraries for a source of a full-length clone, DNA from the libraries was

5 translational initiation site at nucleotide positions 195-197, and a stop signal at nucleotide positions 1077-1079 230-233; potential tyrosine kinase phosphorylation sites at about amino acids 3-11 and 129-136; potential N-42, 57-85, 94-116, and 230-257; potential N-glycosylation sites at about amino acids 118-121, 1899-192, and include: a signal sequence at about amino acids 1-44; possible transmembrane domains at about amino acids 22molocular weight of approximately 33,211 dations and an extimated pl of approximately 5.35 Additional features (Figure 69; SEQ ID NO:122). The predicted polypeptide precursor is 294 amino acids long has a calculated A full length clone was identified that contained a single open reading frame with an apparent

2 between the PRO1311 amino acid sequence and the following Dayhoff sequences: AF065389_1, AF053455_1 CD63_HUMAN, A15_HUMAN, AF043906_1, C151_HUMAN, AF053453_1, AF054838_1, P_R91446, and alignment analysis of the full-length sequence shown in Figure 70 (SEQ ID NO:123), evidenced some homology 287-292; and a cell attachment sequence at about amino acids 3-5. An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

myristoylation sites at about amino acids 80-85, 109-114, 180-185, 218-223, 248-253, 276-281, 285-290, and

deposit no. 203251. Clone DNA64863-1573 was deposited with the ATCC on September 9, 1998, and is assigned ATCC

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CD82_HUMAN

EXAMPLE 39: Isolation of cDNA clones, Encoding Human PRO1357

30 25 Scaule, Washington). The consensus sequence obtained therefrom is herein designated DNAS6034. databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmacenticals, Palo Alto or BLAST2 (Alishul et al., Methods in Enzymology, 266:460-480 (1996)). Those comparisons resulting in a CA) to identify existing homologies. The homology search was performed using the computer program BLAST assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and cluster sequence from the incyte database, designated incyte EST cluster sequence no. 69537. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 71 and is herein designated within the Incyte EST clone no. 936239, the Incyte EST clone no. 936239 was purchased and the cDNA insert In light of the sequence homology between the DNA56034 sequence and an EST sequence contained

The predicted polypeptide precursor is 484 amino acids long (Figure 72). The full-length PRO1357 protein site at mucleotide positions 74-76 and ending at the stop codon at nucleotide positions 1526-1528 (Figure 71). Clone DNA64881-1602 contains a single open reading frame with an apparent translational initiation

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proteins from about amino acid 407 to about amino acid 457. Close DNA64881-1602 has been deposited with about amino acid 415 and an amino acid sequence block having homology to the LBP/BPI/CETP family of ATCC on September 9, 1998 and is assigned ATCC deposit no. 203240. amino acid 401 to about amino acid 404, a glycosaminoglycan attachment site from about amino acid 412 to of the full-length PRO1357 sequence shown in Figure 72 (SEQ ID NO:128) evidences the presence of the shown in Figure 72 has an estimated molecular weight of about 52,468 dations and a pl of about 7.14. Analysis about amino acid 48 to about amino acid 51, from about amino acid 264 to about amino acid 267 and from about following: a signal peptide from abour amino acid 1 to about amino acid 21, potential N-glycosylation sites from

5 homology between the PRO1357 amino acid sequence and the following Dayhoff sequences: MMU46068_1, S17447, MMUI_1, BPI_RABIT, P_W16808, P_R21844, PSP_MOUSE, HSLBPEXI_1 and BTU79413_1. alignment analysis of the full-length sequence shown in Figure 72 (SEQ ID NO:128), evidenced significant An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

EXAMPLE 40: Isolation of cDNA clones Encoding Human PRO1244

20 7 cluster sequence from the LIFESEQ® database, designated cluster no. 7874. This EST cluster sequence was then the computer program BLAST or BLAST? (Alushul et al., Methods in Enzymology 266:460-480 (1996)). Those designated "DNAS6011". University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known from a library constructed from tissue of the corpus cavernosum. The homology search was performed using Geneatech, South San Francisco, CA) to identify existing homologies. One or more of the ESTs was derived GenBank) and a proprietary EST DNA databases (LIFESEQ?, Incyte Pharmaceuticals, Palo Alto, CA compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g. Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

designated "DNA64883-1526". and sequenced. The sequence of this cDNA insert is shown in Figure 73 (SEQ ID NO:129) and is herein within Incyre EST No. 3202349, the EST clone no. 3202349 was purchased and the cDNA insert was obtained In light of the sequence homology between the DNAS6011 sequence and an EST sequence contained

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ઝ glyonsylation stres at about artino acids 71-74, and 215-218; and a cell attachment sequence at about artino acids translational initiation site at nucleotide positions 9-11 and ending at the stop codon found at nucleotide positions is 335 amino acids long. PRO1244 has a calculated molecular weight of approximately 38,037 daltons and an 1014-1016 (Figure 73; SEQ ID NO:129). The predicted polypeptide presursor (Figure 74, SEQ ID NO:130) estimated pl of approximately 9.87. Other features include a signal peptide at about amino acids 1-29. transmembrane domains at about amino acids 183-205, 217-237, 271-287, and 301-321; potential N-The full length clone shown in Figure 73 contained a single open reading frame with an apparem

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An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

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between the PRO1244 amino acid sequence and the following Dayhoff sequences: AF008554_1, P_485334, G02297, HUMN33S11_1, HUMN33S10_1, YO13_CAEEL, GEN13255, S49758, E70107, and ERP5_MEDSA. alignment analysis of the full-length sequence shown in Figure 74 (SEQ ID NO:130), revealed homology

deposit no. 203253 Clone DNA64883-1526 was deposited with the ATCC un September 9, 1998, and is assigned ATCC

EXAMPLE 41: [solation of cDNA clones Encoding Human PRO1246

5 5 Scattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56021. BLAST score of 70 (or in some cases 90) or greater that did not encode known proceins were clustered and or BLAST2 (Altabul et al., Methods in Enzymology, 266:460-480 (1996)). Those comparisons resulting in a CA) to identify existing homologics. The homology search was performed using the computer program BLAST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 56853. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

as DNA64885-1529. was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 75 and is herein designated within the Incyte EST clone no. 2481345, the Incyte EST clone no. 2481345 was purchased and the cDNA insert In light of the sequence homology between the DNA56021 sequence and an EST sequence contained

30 z 20 about amino acid 286 to about amino soid 315, from about amino acid 359 to about amino acid 369 and from acid 375 to about amino acid 378, from about amino acid 413 to about amino acid 416 and from about amino about amino acid 108 to about amino acid 111, from about amino acid 166 to about amino acid 169, from about following: a signal peptide from about amino acid 1 to about amino acid 15, potential N-glycosylation sites from of the full-length PRO1246 sequence shown in Figure 76 (SEQ ID NO:132) evidences the presence of the site at nucleotide positions 119-121 and ending at the stop codon at nucleotide positions 1727-1729 (Figure 75) November 3, 1998 and is assigned ATCC deposit no. 203457. about amino acid 78 to about amino acid 97. Clone DNA64885-1529 has been deposited with ATCC on acid 498 to about amino acid 501 and amino acid sequence blocks having homology to sulfatuse proteins from amino acid 193 to about amino acid 196, from about amino acid 262 to about amino acid 265, from about amino shown in Figure 76 has an estimated molecular weight of about 61,450 daltons and a pl of about 9.17. Analysis The predicted polypeptide precursor is 536 amino acids long (Figure 76). The full-length PRO1246 protein Clone DNA64885-1529 contains a single open reading frame with an apparent translational initiation

35 CELK09C4_1, BCU448S2_1, IDS_HUMAN, G65169, E64903, ARSA_HUMAN, GL6S_HUMAN homology between the PRO1246 amino acid sequence and the following Dayhoff sequences: P_R51355 IISARSF_1 and GEN12648. alignment analysis of the full-length sequence shown in Figure 76 (SEQ ID NO:132), evidenced significant An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

EXAMPLE 42: Isolation of cDNA clones Encoding Human PRO1356

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence to the theory of expressed sequence to the first cluster sequence on the factor of the theory of expressed sequence to g (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifester, Incyle Pharmaceuticals, Polo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST (Altabul et al., Methods in Enzymology Search was performed using the computer program BLAST acree of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is berein designated DNA55023.

10 In light of the sequence homology between the DNA\$6023 sequence and an EST sequence contained within the Incyre EST clone no. 4071746, the Incyre EST clone no. 4071746 was purchased and the cDNA basen was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 77 and is herein designated as DNA\$4886-1601.

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Clone DNA64886-1601 contains a single open reading frame with an apparent translational initiation 15 site at nucleotide positions 122-124 and ending at the stop codon at nucleotide positions 812-814 (Figure 77).

The predicted polypeptide precursor is 230 amino acids long (Figure 78). The full-length PRO1356 procein shown in Figure 78 has an estimated molecular weight of about 24,549 datons and a pt of about 8.56. Analysis of the full-length PRO1356 acquence shown in Figure 78 (SEQ ID NO:134) evidences the presence of the following: a signal peptide from about amino acid 10 about amino acid 24, transmembrane domains from about amino acid 82 to about amino acid 102. from about amino acid 117 to about amino acid 140 and from about amino acid 163 to about amino acid 182, a potential N-glycosylation site from about amino acid 190 to about amino acid 190 and an amino acid sequence block having homology to the PMP-22/EMP/MP20 family of proteins from about amino acid 46 to about amino acid 59. Clone DNA64886-1601 has been deposited with ATCC on September 9, 1998 and is assigned ATCC deposit no. 203241.

An analysis of the Dayhoff database (version 35.45 SwissPort 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 78 (SEQ ID NO:134), evidenced significant homology between the PRO1356 amino acid sequence and the following Dayhoff sequences: AB00014_1, AB000712_1, A39484, AF000959_1, AF035814_1, HSU89916_1, MMU19582_1, P_R30059, HUACD04125_1 and PM22 RAT.

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EXAMPLE 43: Isolation of CDNA clones Encoding Human PRO1275

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A novel secreted molecule, designated herein as DNAS7700, was used to BLAST against Incyte's (LIFESBQ*, Incyte Pharmaceuticals, Palo Alto, CA) proprietary database and Genbank's public database. Positive clones were identified and used to generate assembly files by sequent program. The search was performed using the computer program BLAST or BLAST2 [Altschall et al., Methods in Enzymology, 266:460 480 (1996)] as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known.

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proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green University of Washington, Seattle, Washington).

A consensus DNA sequence was assembled relative to other EST sequences using repeated cycles of BLAST and phrap. This consensus sequence is designated herein "DNA59572".

Based on the DNA59572 consensus sequence and its relation to sequences identified in the assembly,

5 one of the clones (Incyte clone 2026581) including one of the sequences in the assembly was purchased and
sequenced. Incyte clone 2026581 came from a library constructed of RNA from epidermal breast keratinocytes.

The entire coding sequence of PRO1275 is shown in Figure 79 (SEQ ID NO:135). Clone DNA648881542 comains a single open reading frame with an apparent translational Indiation site at nucleotide positions
37-39 and an apparent stop codon at nucleotide positions 394-396 of SEQ ID NO:135. The predicted
10 polypeptide precursor is 119 amino acids long. The signal peptide is at about amino acids 1-25 of SEQ ID
NO:136. Clone DNA64888-1542 has been deposited with ATCC and is assigned ATCC deposit no. 203249.

The full-length PRO1275 protein shown in Figure 79 has an estimated molecular weight of about 13,248 dahous and a pl of about 7.78.

An analysis of the Dayboff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence 15 alignment analysis of the full-length sequence shown in Figure 80 (SEQ ID NO:136), revealed sequence identity between the PRO1275 amino acid sequence and the following Dayboff sequences (information from database incorporated herein): B48151 (Mst98Cb), D86424_1 (htgh-stiffur keratin protein), P_R79964 (connective tissue growth factor), CHRD_RAT (chordin), MT_DREPO (metallothionein), PLDS_PLETR (piccoxins), P_R25156 (Ig antigen), S73732_1 (VLDP), AF025440_1 (OIP4) and P_R32757 (IGF-ID).

EXAMPLE 44: Isolation of cDNA clones Encoding Human PRO1274

A novel secreted molecule, designated herein as DNAST700, was used to blast against lacyte's (LIFESEQ*, incyte Pharmaceuticals, Palo Alto, CA) proprietary database and Genbank's public database. Positive clones were identified and used to generate assembly files by seqext program. The search was performed using the computer program BLAST or BLAST7 [Altschul et al., Methods in Enzymology, 266:460, 480 (1996)] as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green,

30 A consensus DNA sequence was assembled relative to other EST sequences using repeated cycles of BLAST and phrap. This consensus sequence is designated herein "DNA59573".

University of Washington, Seattle, Washington).

Based on the DNA59573 consensus sequence and its relation to sequences identified in the assembly, one of the clones (Incyte clone 2623992) including one of the sequences in the assembly was purchased and sequenced. Incyte clone 2623992 came from a library constructed of RNA from epidermal breast keratinocytes.

The entire coding sequence of PRO1274 is shown in Figure 81 (SEO ID NO-127). Close DNASCHOOL.

The entire coding sequence of PRO1274 is shown in Figure 81 (SEQ ID NO:137). Clone DNA648891541 contains a single open reading frame with an apparent translational initiation site at nucleotide positions
24-26, and an apparent stop codon at nucleotide positions 354-356 of SEQ ID NO:137. The predicted

PRO1274 protein shown in Figure 82 has an estimated molecular weight of about 12,363 daltons and a pI of DNA64889-1541 has been deposited with ATCC and is assigned ATCC deposit no. 203250. The full-length Conserved regions in the insulin family of proteins and an N-glycosylation site are indicated in Figure 82. Clone solypeptide precursor is 110 amino acids long. The signal peptide is at about 1-24 of SEQ ID NO:138

ö CXMI_CONGE,-P_P61301, TXA4_RADMA (neurotoxin 4). BTIGF2REC_1 (insulin-like growth factor 2). HSNF1GEN12_1, TXA3_RADMA (neurosoxin incorporated herein): CEW05B2_9, AP016922_1 (insulin-like growth factor 1), B48151, A53640, alignment analysis of the full-length sequence shown in Figure 82 (SEQ ID NO: 138), revealed sequence identity between the PRO1274 amino acid sequence and the following Dayhoff sequences (information from database An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

EXAMPLE 45: Isolation of cDNA clones Encoding Human PRO1412

2 encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was derived from RNA therefrom is herein designated "DNA58754". isolated from fibroblasts of the prostate stroma removed from a male fetus. The consensus sequence obtained 480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not performed using the computer program BLAST or BLAST2 (Alishul et al., Methods in Enzymology 266:460 (LIFESEQ®, Incyte Pharmaceuteals, Paio Alto, CA) to identify existing homologies. The homology search was databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database "DNA10643". This EST chaster sequence was then compared to a variety of expressed sequence tag (EST) cluster sequence from the LIFESEQ* database, designated Incyte Cluster No. 101368, also referred herein as Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

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within EST no. 3597385, the EST clone 3597385 was purchased and the cDNA insert was obtained and sequenced in its entirety. The sequence of this cDNA insert is shown in Figure 83 and is herein designated as In light of the sequence homology between the DNAS8754 sequence and an EST sequence contained

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35 y positions 1075 to 1077 (Figure 83; SEQ ID NO:139). The predicted polypeptide precursor (Figure 84, SEQ amino acids 183-224. PRO1412 has a calculated molecular weight of approximately 33,908 dathors and an slic at about amino acids 62-69; and a lysosome-associated membrane glycoprotein duplicated domain at about ID NO:140) is 311 amino acids long. Other features of the PRO1412 protein include: a signal sequence at about about amino acids 49-52, 91-94, 108-111. 128-131, 135-138 and 190-193; a tyrosine kinase phosphorylation amino acids 1-28; a transmembrane domain at about amino acids 190-216; potential N-glycosylation sries at translational initiation site at nucleotide positions 142 to 144 and ending at the stop codon found at nucleotide 1998, and is assigned ATCC deposit no. 203216. estimated pl of approximately 6.87. Clone DNA64897-1628 was deposited with the ATCC on September 15. The full length clone shown in Figure 83 contained a single open reading frame with an apparent

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NCA2_RAT. 161783. P_W07682, MMHC135G15_3, S21461, MMIGL2_1, ONHIGMY9A_1 and between the PRO1412 amino acid sequence and the following Dayhoff sequences: 150116, AF035963_1, alignment analysis of the full-length sequence shown in Figure 84 (SEQ ID NO:140), revealed some homology An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

EXAMPLE 46: Isolation of cDNA clones. Encoding Human PRO1557

5 Washington). The consensus sequence obtained from the assembly is herein designated "DNA58763". existing homologies. The homology search was performed using the computer program BLAST or BLAST2 of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score variety of expressed sequence tag (EST) databases, which included the EST databases listed above, to identify consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, sequence from the Geneniech database, designated "DNAS8763. This EST sequence was then compared to a Use of the signal sequence algorithm described in Example 3 above allowed identification of an ESI

2 The sequence of this cDNA insert is shown in Figure 85 and is herein designated as DNA64902-1667. within the EST no. 2267403, EST no. 2267403 was purchased and the cDNA insert was obtained and sequenced. In light of the sequence homology between the DNA58763 sequence and an EST sequence contained

25 20 about amino acids 54-49, 66-71, 146-151, and 367-372; potential amidation sites at about amino acids 36-39 and ID NO:142) is 451 amino acids long. PRO1557 has a calculated molecular weight of approximately 49,675 positions 1640 to 1642 (Figure 85; SEQ ID NO:141). The predicted polypeptide precursor (Figure 86, SEQ 205-208; and an ATP/GTP-binding site motif A (P-toop) at about amino acids 151-258. dependent protein kinase phosphorylation site at about amino acids 388-41; potential N-myristoylation sites at acids 1-25; a potential N-glycosylation site at about amino acids 114-117; a potential cAMP and cGMPdaltons and an estimated pl of approximately 7.15. Additional features include: a signal sequence at about amino translational initiation site at nucleotide positions 287 to 289 and ending at the stop codon found at nucleotide The full length clone shown in Figure 85 contained a single open reading frame with an apparent

30 found between the PRO1557 amino acid sequence and the following Dayhoff sequences: P_W31559 AF031230_1, SOG_DROME, CA11_MOUSE, P_R41320, CHRD_RAT, P_W40288, NEL_CHICK, and homology between the PRO1557 amino acid sequence and Dayhoff sequence AF034606_1. Homology was also alignment analysis of the full-length sequence shown in Figure 86 (SEQ ID NO:142), revealed significant An analysis of the Dayhoff thatabase (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

deposit no. 203317. Clone DNA64902-1667 was deposited with the ATCC on October 6, 1998, and is assigned ATCC

EXAMPLE 47: Isolation of cDNA clones Encoding Human PRO1286

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

cluster sequence from the LIFESEQ® database, designated EST Cluster No. 86809. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyto Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Engarmology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). ESTs in the assembly included those identified from tumors, cell lines, or diseased issue.

10 In light of the sequence homology between the DNA 58822 sequence and an EST sequence contained within EST no. 1695434, EST clone no. 1695434 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 87 and is herein designated DNA64903-1533 (SEO ID NO-143)

tissue. The consensus sequence obtained therefrom is herein designated DNA58822.

One or more of the ESTs was obtained from a cDNA library constructed from RNA isolated from diseased colon

The full length close shown in Figure 87 contained a single open reading frame with an apparent 15 translational initiation site at nucleotide positions 93-95 and enaling at the stop codor found at nucleotide positions 372-374 (Figure 87; SEQ ID NO:143). The predicted polypeptide precursor (Figure 88, SEQ ID NO:144) is 93 amino acids long, with a signal sequence at about amino acids 1-18. PRO1286 has a calculated molecular weight of approximately 10,111 dations and an estimated pl of approximately 9.70.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WUL-BLAST2 sequence 20 alignment analysis of the full-length sequence shown in Figure 88 (SEQ ID NO:144), revealed some homology between the PRO1286 amino acid sequence and the following Dayhoff sequences: SR5C_ARATH, CELC17H12_II, MCPD_ENTAE, JQ2283, INVO_LEMCA, P_R07309, ADEVBCAGN_4, AFD20947_I, CELT73H2_I, and MDH_STRAR.

Close DNA64903-1553 was deposited with the ATCC on September 15, 1998 and is assigned ATCC deposit no. 200223,

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EXAMPLE 48: Isolation of cDNA clones Encoding Human PRO1294

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the ineyte database, designated fncyte EST cluster sequence no. 10559. This EST cluster 30 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ*, Incyte Pharmacounicals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus DNA sequence obtained therefrom is betein designated DNA57203.

In light of the sequence homology between the DNA57203 sequence and an EST sequence contained

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within the Incyte EST clone no. 3037763, the Incyte EST clone no. 3037763 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 89 and is herein designated as DNA64905-1558.

Clone DNA64905-1538 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 110-112 and ending at the stop codon at nucleotide positions 1228-1330 (Figure 89).

5 The predicted polypoptide precursor is 406 amino acids long (Figure 90). The full-length PRO1234 protein shown in Figure 90 has an estimated molecular weight of about 46,038 dattons and a p1 of about 6.50. Analysis of the full-length PRO1234 sequence shown in Figure 90 (SEQ ID NO:146) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21 and potential N-glycosylation sites from about amino acid 177 to about amino acid 180 and from about amino acid 248 to about amino acid 251.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 90 (SEQ ID NO:145), evidenced significant homology between the PRO1294 amino acid sequence and the following Dayhoff sequences: I73636,

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во. 203233.

Clone DNA64905-1558 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit

15 AF028740_1, AB00668653_1, P_R98225, RNU78105_1, CELC48E7_4, CEF11C3_3, SCP1_MESAU, TPM3_HUMAN and CELX0582_3.

EXAMPLE 49: Isolation of cDNA clones Encoding Human PRO1347

A consensis DNA sequence was assembled relative to other EST sequences using phrap as described 20 in Example 1 above. This consensus sequence is designated herein "DNA47373". Based on the DNA47373 contensus sequence, oligomocleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1347.

PCR primers (forward and reverse) were synthesized:

25 forward PCR primet 5'GCGTGGTCCACCTCTACAGGGACG3' (SEQ ID NO:149); and textise PCR primet 5'GGAACTGACCCAGTGCTGACACCG3' (SEQ ID NO:150).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47373 sequence which had the following nucleotide sequence:

http://dizaiton.probe.5'GCAGATGCCACAGTATCAAGGCAGGACAAAACTGGTGAAGGATTC3' (SEQ ID 30 NO:151).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A postive library was then used to isolate clones encoding the PRO1347 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human small intestine.

35 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1347 and the derived protein sequence for PRO1347.

The entire coding sequence of PRO1347 is shown in Figure 91 (SEQ ID NO: 147). Clone DNA64950.

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1500 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 183-185, and an apparent stop codon at nucleotide positions 1683-1685 of SEQ ID NO:147. The predicted polypeptide precursor is 500 amino acids long. The signal peptide is at about amito acids 1-17 and the transmembrane dumain is at about 239-255 of SEQ ID NO:148. Clone DNA64950-1590 has been deposited with ATCC and is assigned ATCC deposit no. 203224. The full-length PRO1347 protein shown in Figure 92 has an estimated molecular weight of about 56,748 daltons and a p1 of about 8.5.

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An analysis of the Dayhoff dambase (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 92 (SEQ ID NO:148), revealed sequence identity between the PRO1347 amino acid sequence and the following Dayhoff sequences (data incorporated herein): BUTY_HUMAN, AF033107_1, HSU90142_1, HSU90144_1, HSB73_1, HS111M5_2, ROS2_HUMAN, AF03800_1, HSAJ03147_4, and MOG_MOUSE.

EXAMPLE 30: Isolation of cDNA clones Encoding Human PRO1305

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A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA38103. Based on the DNA38103 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1305.

PCR primers (forward and reverse) were synthesized:

20 ENERS FCR primer [38/03.11) 5'-AACTGCTGTGGGTTGGAAGCCTG-3' (SEQ ID NO:154)
Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA38103 requence which had the following nucleotide sequence

5'-AGGTTATCAGGGGCTTCACTGTGAAACCTGCAAAGAGG-3' (SEQ ID NO:156)

hybridization probe (38103.p1)

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In order to seceen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1305 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal hidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1305 (designated herein as DNA64952-1568 [Figure 93, SEQ ID NO:152]; and the derived protein

The entire nucleotide sequence of DNA64952-1568 is shown in Figure 93 (SEQ ID NO:152). Close DNA64952-1568 contains a single open reading frame with an apparent translational initiation site at mediotide positions 126-128 and ending at the stop codon at nucleotide positions 900-902 (Figure 93). The predicted positions 126-128 and ending at the stop codon at nucleotide positions 900-902 (Figure 93). The predicted positions 900-902 (Figure 93). The full-length PRO1305 protein shown in Figure 94 (SEQ ID NO:153) evidences the presence of the following: a signal PRO1305 sequence shown in Figure 94 (SEQ ID NO:153) evidences the presence of the following: a signal

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peptide from about amino acid 1 to about amino acid 25, potential N-glycosylation sites from about amino acid 20 to about amino acid 30 to about amino acid 33, from about amino acid 172 to about amino acid 175, from about amino acid 198 to about amino acid 198, from about amino acid 208 to about amino acid 211 and from about amino acid 235 to about amino acid 238 and an EGF-like domain cystetic pattern signature sequence from about amino acid 214 to about amino acid 225. Clone DNA64952-1568 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203222.

An analysis of the Dayhoff database (version 35.45 SwitsProt 35), using a WU-BLAST2 sequence alignment studysis of the full-length sequence shown in Figure 94 (SEQ ID NO:153), evidenced significant homology between the PRO1305 amino acid sequence and the following Dayhoff sequences: CET22A3.7, LMA2_MOUSE, AFD55580_1, AF016903_1, LMB2_MOUSE, P_R71730, LMB3_MOUSE, LMG1_HUMAN;

10 LMGI_DROME and LMAS_MOUSE. As such, the PRO1305 polypeptide does show homology to laminin and may be a laminin homolog.

EXAMPLE 51: Isolation of cDNA clones Enceding Human PRO1273

An expressed sequence tag (EST) DNA database (LIFESEQ*, Incyte Pharmaceuticals, Palo Alto, CA)

was searched and an EST was identified. This sequence was blazed against public databases and Incyte's
database. The search was performed using the computer program BLAST or BLAST2 (Altachul et al., Methods
in Enzymplogy, 266:460-480 (1996)] as a comparison of the extraochular domain (ECD) protein sequences to
a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some
cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA

20 sequences with the program 'phrap' (Phil Green, University of Washington, Seattle, Washington).

A consecute DNA sequence was assembled relative to other EST sequences using repeated cycles of BLAST and phrap. This consensus sequence is designated herein 'DNA60747'. Based on the DNA60747 consensus sequence and its relation to a sequence within the assembly of aligned sequences, lacyte clone 3541105 was purchased and sequenced in full. This lacyte clone came from a library constructed of RNA 25 isolated from seminal vesicle tissue.

The entire coding sequence of PRO1273 is shown in Figure 95 (SEQ ID NO:157). Clone DNA65402.

1540 contains a single open reading frame with an apparent translational initiation site at nucleotide positions

26-28 and an apparent stop codon at nucleotide positions 515-517 of SEQ ID NO:157. The predicted

polypeptide precursor is 163 amino acids long. The signal peptide is at about amino acids 1-20 and the

30 conserved region in lipocalins is at about amino acids 23-36 of SEQ ID NO:158. Clone DNA65402-1540 has been deposited with ATCC and is assigned ATCC deposit no. 203252. The full-length PRO1273 protein shown in Figure 96 has an estimated molecular weight of about 18,045 dations and a p1 of about 4.87.

An analysis of the Dayhoff database (version 35.45 SwitsProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 96 (SEQ ID NO:158), revealed sequence identity between the PRO1273 amino acid sequence and the following Dayhoff sequences (information from database incorporated herein): PGHD_FELCA (prostaglandin-b2 d-isomerase precursor), SS7748 (prostaglandin D synthetase precursor), LIPO_BUFMA (tipocalin precursor), SS2354, QSP_CHICK, ECP19_1, LACB_CAPHI,

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OLFA_RANPI, D87752_I, and LACB_BOVIN

EXAMPLE 52: Isolation of cDNA clones Encoding Human PRO 1302

A consensus DNA sequence encoding PRO1302 was assembled relative to other EST sequences using repeated cycles of phrap as described in Example 1 above. This consensus sequence is designated herein "DNA28742". Based on the DNA28742 consensus sequence, the assembly from which the consensus sequence was derived and other information and discoveries provided herein, the Incyto clone 3344926 (from a discassed spleen tissue library) was purchased and sequenced in full. Sequencing provided the full-length DNA sequence for PRO1302 and the derived protein sequence for PRO1302.

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The entire coding sequence of PRO1302 is shown in Figure 97 (SEQ ID NO:159). Clone DNA654031565 contains a single open reading frame with an apparent translational initiation site at nucleotide positions
43-45 and an apparent stop codon at nucleotide positions 1432-1435 of SEQ ID NO:159. The prodicted
polypeptide precursor is 463 amino acids long. The signal peptide is at about amino acids 1-15 and the
transmembrane sequence is at about amino acids 351-370 of SEQ ID NO:160. Clone DNA65403-1565 has been
deposited with the ATCC and is assigned ATCC deposit no. 207230. The full-length PRO1302 protein shown
in Figure 98 has an estimated molecular weight of about 50,082 daltons and a pl of about 7.3.

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An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLASTZ sequence alignment analysis of the full-length sequence shown in Figure 98 (SEQ ID NO:160), revealed sequence identify between the PRO1302 amino acid sequence and the following Dayhoff sequences (data incorporated herein): D86358_1,D86359_1,S71403_1,MAG_HUMAN,HO593,MMSIAL2_1,C22A_HUMAN,PGBM_HUMAN, PGBM_HUMAN,LACH_DROME, and KMLS_HUMAN.

EXAMPLE 53: Isolation of cDNA clones Encoding Human PRO1283

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A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA28753. Based on the DNA28753 consensus sequence, oligonucleotides were symbesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1283.

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PCR primers (forward and reverse) were synthesized:

Invard PCR primer (28753.11) 5'-GGAGATGAAGACCCTGTTCCTG-3' (SEQ ID NO:163)

[Invard PCR primer (28753.11) 5'-GGAGATGAAGACCCTGTTCCTGGGTG-3' (SEQ ID NO:164)

[Invard PCR primer (28753.11) 5'-GTCCTCCGGAAAGTCCTTATC-3' (SEQ ID NO:165)

[Invard PCR primer (28753.11) 5'-GCCTAGTGTTCGGAAAGTCCTTATC-3' (SEQ ID NO:166)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA28753 sequence which had the following nucleotide sequence

hybridization probe (28753.p1)

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5'-CAGGGACCTGGTACGTGAAGGCCATGGTGGTCGATAAGGACTTTCCGGAG-3' (SEQ ID NO:167)
hvbidizaion broks (2275).pl1).

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5'-CTGTCCTTCACCCTGGAGGAGGAGGATATCACAGGGACCTGGTAC-3' (SEQ ID NO:168)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate cloues encoding the PRO1283 gene using the probe oligonacleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast tumor tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1283 (designated herein as DNA65404-155) [Figure 99, SEQ ID NO:161]; and the derived protein sequence for PRO1283.

The entire nucleotide sequence of DNA65404-1551 is shown in Figure 99 (SEQ ID NO:161). Clone DNA65404-1551 contains a single open reading frame with an apparent translational initiation site at mucleotide 10 positions 45-47 and ending at the stop codon at nucleotide positions 555-557 (Figure 99). The predeted polypeptide precursor is 170 amino acids long (Figure 100). The full-length PRO1283 protein shown in Figure 100 has an estimated molecular weight of about 19,457 dattons and a p1 of about 9.10. Analysis of the full-length PRO1283 sequence shown in Figure 100 (SEQ ID NO:162) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 17. Clone DNA65404-1551 has been deposited with 15. ATCC on September 9, 1998 and is assigned ATCC deposit no. 203244

An analysis of the Dayhoff darabase (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 100 (SEQ ID NO:162), evidenced significant bomoology between the PRO1283 amino acid sequence and the following Dayhoff sequences: A40464, VEGP_HUMAN, ALL1_CANFA, LALP_TRIVU, S51803, XELPDS_1, LIPO_BUFMA, S52354, QSP_CHICK and ERBP_RAT.

EXAMPLE 54: Isolation of cDNA clones Encoding Human PRO1279

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A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA30856. Based on the DNA30856 consensus sequence, oligonucleorides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO12719.

PCR primers (forward and reverse) were synthesized:

35 Additionally, synthetic oligonucleotide hybridization probes were constructed from the consenus DNA30856 sequence which had the following nucleotide sequences: hybridization probe [20856.p1].

S'-AGGCCATGAGGATTCTGCAGTTAATCCTGCTTGCTCTGGCAACAGGGCTT-3' (SEQ ID NO:177)

5'-GAGAGACCAGGATCATCAAGGGGTTCGAGTGCAAGCCTCACTC-3' (SEQ ID NO:178)

isolate clanes encoding the PRO1279 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human lung tumor tissue. screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to In order to screen several libraries for a source of a full-length clone. DNA from the libraries was

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PRO1279 (designated herein as DNA65405-1547 [Figure 101, SEQ ID NO:169]; and the derived protein DNA sequencing of the clours isolated as described above gave the full-length DNA sequence for

23 20 2 5 from about amino acid 222 to about amino acid 249 and from about amino acid 189 to about amino acid 222. Clone DNA65405-1547 has been deposited with ATCC on November 17, 1998 and is assigned ATCC deposit proteins from about amino acid 197 to about amino acid 209 and from about amino acid 47 to about unino acid no. 203476 site from about amino acid 145 to about amino acid 148, amino acid sequence blocks present in kringle domain length PRO1279 sequence shown in Figure 102 (SEQ ID NO:170) evidences the presence of the following: a 64, amino acid sequence blocks having homology to serine protease, trypsin family, histidine proteins from about DNA65405-1547 contains a single open reading frame with an apparent translational initiation site at nucleotide acid 220 to about amino acid 243 and amino acid sequence blocks having bomology to apple domain proteins amino acid 199 to about amino acid 209, from about amino acid 47 to about amino acid 63 and from about amino about amino acid 184 and from about amino acid 210 to about amino acid 213, a glycosaminoglycan anachment to about amino acid 102, from about amino acid 165 to about amino acid 168, from about amino acid 181 to site from about amino acid 38 to about amino acid 63, potential N-glycosylation sites from about amino acid 99 signal peptide from about amino acid 1 to about amino acid 18, a serine protease, trypsin family, histidine active 102 has an estimated molecular weight of about 27,466 daltons and a pl of about 8.87. Analysis of the fullpolypeptide precursor is 250 amino acids long (Figure 102). The full-length PRO1279 protein shown in Figure positions 106-108 and ending at the stop codon at nucleotide positions 856-858 (Figure 101). The predicted The entire nucleotide sequence of DNA65405-1547 is shown in Figure 101 (SEQ ID NO:169). Clone

homology between the PRO1279 amino acid sequence and the following Dayhoff sequences: 156559, SS5066, KLK7_RAT, KLK1_RAT, KLK8_RAT, KLK3_MOUSE, KLK8_RAT, AF013988_1, D78203_1 and alignment analysis of the full-length sequence shown in Figure 102 (SEQ ID NO:170), evidenced significant An analysis of the Dayboff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

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NO:169) sequencing the insert of that done, thereby giving the DNA65405-1547 sequence shown in Figure 101 (SEQ ID Additionally, DNA63405-1547 was obtained by purchasing the Incyre EST clone no. 2723646 and

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EXAMPLE 55: Isolation of cDNA clones Encoding Human PRO1304

the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for in Example 1 above. This consensus sequence is herein designated DNA35745. Based on the DNA35745 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that coutained A consensus DNA sequence was assembled relative to other EST sequences using plurap as described

PCR primers (forward and reverse) were synthesized:

forward PCR primer (35745.12) forward PCR primer (35745.ft) 5'-GTGTTCTGCTGGAGCCGATGCC-3' (SEQ ID NO:181) 5'-GACATGGACAATGACAGG-3' (SEQ ID NO:182)

forward PCR primer (35745.f3) 5'-CCTTTCAGGATGTAGGAG-3' (SEQ ID NO:183)

5 reverse PCR primer (35745.r2) 5'-TACAAGAGGGAAGAGGGGGTTGCAC-3' (SEQ ID NO:186) teverse PCR primer (35745,[]) forward PCR primer (35745.f4) 5'-OCATCCTGATATGACTTGTCACGTGGC-3' (SEQ ID NO:185) 5'-GATGTCTGCCACCCCAAG-3' (SEQ ID NO:184)

15 hybridization probe (35745.pl)

sequence which had the following nucleotide sequence

additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35745

20 screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to 5'-GCCCATTATGACGGCTACCTGGCTAAAGACGGCTCGAAATTCTACTGCAGCC-3(SEQ ID NO: 187) isolate clones encoding the PRO1304 gene using the probe oligonucleotide and one of the PCR primers. RNA In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

sequence for PRO1304. PRO1304 (designated herein as DNA65406-1567 [Figure 103, SEQ ID NO:179]; and the derived protein DNA sequencing of the clones isolated as described above gave the full-length DNA sequence to for construction of the cDNA libraries was isolated from human ovary tissue.

30 25 DNA65406-1567 contains a single open reading frame with an apparent translational initiation site at nucleotide to about amino acid 142 and EF-hand catcium binding domain protein homology blocks from about amino acid endoplasmic reticulum targeting sequence from about amino acid 219 to about amino acid 222, a potential Nisomerase bemology blocks from about amino acid 87 to about amino acid 123 and from about amino acid 129 glycosylation site from about amino acid 45 to about amino acid 48, FKBP-type peptidyl-prolyl cis-trans length PRO1304 sequence shown in Figure 104 (SEQ ID NO:180) evidences the presence of the following: an 104 has an estimated molecular weight of about 25,794 daltons and a pl of about 6.24. Analysis of the fullpolypeptide precursor is 222 amino acids long (Figure 104). The full-length PRO1304 protein shown in Figure positions 23-25 and ending at the stop codon at nucleotide positions 689-691 (Figure 103). The predicted The entire nucleotide sequence of DNA65406-1567 is shown in Figure 103 (SEQ ID NO:179). Clone

35 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203219. 202 to about amino acid 214 and from about amino acid 195 to about amino acid 214. Clone DNA65406-1567

alignment analysis of the full-length sequence shown in Figure 104 (SEQ ID NO:180), evidenced significan An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

homology between the PRO1304 amino acid sequence and the following Dayhoff sequences: AF040252 1, P_R28980, S71238, CELC05C8_1, VFU52045_1, S75144, FKB3_BOVIN, CELC50F2_6, CELB0511_12 and P_R41781.

The DNA65406-1567 sequence was also obtained by isolating and sequencing the insert of Incyte EST tone no. 2813577.

EXAMPLE 56: Isolation of cDNA clones Encoding Human PRO1317

Using the exchangue described in Example 1 above, Incyte EST no. 33598 was identified as a sequence of interest having a BLAST score of 70 or greater that did not encode a known protein. The sequence of Incyte EST no. 33598 is designated herein as "DNA36958". Based on the DNA36958 sequence, oligonucleonides can be synthesized: 1) to identify by PCR a cDNA library that contains the sequence of interest, and 2) for use as

probes to isolate a clone of the full-length coding sequence for PRO1317.

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The following are suitable PCR primers (forward and reverse) that can be symthesized based on the DNA36938 sequence:

ZEVETSE PCR primer: CGTTACATGTCTCCAAGGGGAATG (36958.1; SEQ ID NO:191)

forward PCR primer: AGGGACCATTGCTTCCTTCCAGGCC (36958.f1; SEQ ID NO:190)

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Additionally, a synthetic oligonucleotide hybridization probe can be constructed from the consensus DNA36958 sequence having the following nucleotide sequence:

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In order to screen several libraries for a source of a full-length clone. DNA from the libraries is screened by PCR amplification with the PCR primer pair identified above. A positive library is then used to isolate clones encoding the PRO1317 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries can be isolated from tissue containing the sequence of interest, for example from peripheral blood, particularly blood taken from a patient having a high leukocyte count (e.g. hypercosinophilia).

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The full-length DNA sequence for PRO1317, designated herein as DNA65408-1578 (Figure 105; SEQ ID NO:188) was obtained by purchasing Incyre EST no. 335958, obtaining the cDNA insert, and sequencing it in its entirety. Incyre clone no. 335958 originated from a library constructed using RNA isolated from peripheral blood cells apheresed from a male patient afflicted with hyperrestinophilia.

The entire coding sequence of PRO1317 is shown in Figure 105 (SEQ ID NO:188). Clane DNA65408.

1578 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 6-8 and an apparent stop codon at nucleotide positions 228-230. The predicted polypeptide precursor is 74 amino acids long. The full-length PRO1317 protein shown in Figure 105 has an estimated molecular weight of about 7,831 daltons and a pl of about 9.08. Additional features include: a signal peptide at about amino acids 51-18, potential N-glycoxylation sites at about amino acids 34-37 and 39-42, and a microbodies C-terminal targeting signal at amino acids 72-74.

An analysis of the Dayhoff dambase (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

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alignment analysis of the full-length sequence shown in Figure 106 (SEO ID NO:189), revealed significant homology between the PRO1317 amino acid sequence and the Dayhoff sequence designated CD97 HUMAN. Additionally, some homology was found between the PRO1317 amino acid sequence and the following Dayhoff sequences: GEN12618, CELZX783_1, G156_PARPR, GIAVSPE_1, AF040387_1, S78059, 150617, XLSEK1_1, and NEL2_RAT.

Clone DNA65408-1578 was deposited with the ATCC on September 15, 1998, and is assigned ATCC deposit no. 203217.

EXAMPLE 57: Isolation of cDNA clones Encoding Human PRO1303

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described
10 in Example 1 above. This contensus sequence is designated herein "DNA47347". Based on the DNA47347
consensus sequence and its homology to an Incyte EST within the assembly from which DNA47347 was derived,
Incyte clone 1430305 (from an iteum tissue library) was purchased and sequenced in full. The sequence
cneeding PRO1303 was thereby identified.

The entire coding sequence of PRO1303 is shown in Figure 107 (SEQ ID NO:193). Clone DNA6540915 1566 contains a single open reading frame with an apparent translational initiation site at macleotide positions
121-123 and an apparent top codon at nucleotide positions 865-867. The predicted polypeptide precursor is 248
amino acids long. The signal peptide is at about amino acids 1-17 of SEQ ID NO:194. The locations of Nglycosylation sites, active and conserved regions and domains are further indicated in Figure 194. Clone
DNA65409-1566 has been deposited with ATCC and is assigned ATCC deposit no. 203232. The full-length
20 PRO1303 protein shown in Figure 108 has an estimated molecular weight of about 26,734 dations and a p1 of

An analysis of the Dayhoff database (version 35.45 SwitssProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 108 (SEQ ID NO.194), revealed sequence identity between the PRO1303 amino acid sequence and the following Dayhoff sequences (data incorporated herein):

25 AB009849_I, P_W08475, AF024605_I, A42048_I, TRY3_RAT, MMAE0006614, TRY1_RAT, MMAE000663_4, MMAE000665_2, and MMAE00066412.

about 7.9.

EXAMPLE 58: Isolation of cDNA clones Encoding Human PRO1306

Using the method described in Example 1 above, Incyte EST No. 2449282, also referred to herein as 30 DNA5918, was identified as a sequence of interest thaving a BLAST acore of 70 or greater that did not encode a known protein. From the DNA5918 sequence, a consensus sequence was assembled using BLAST and the program "phrap" (Phil Green, University of Washington, Scattle, Washington). This consensus sequence is designated herein as "DNA47399". Based on the DNA47399 consensus sequence, oligonucleoides can be synthesized: 1) to identify by PCR a cDNA library that comiains the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1306.

The entire coding sequence of PRO1306 shown in Figure 109 (SEQ ID NO:195), was obtained by purchasing incyre EST no. 2449282, obtaining the cDNA insert and sequencing it in its entirety. Clone

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precursor is 150 amino acids long. The full-length PRO1306 protein shown in Figure 110 has an estimated positions 106-108 and an apparent stop codon at nucleotide positions 556-558. The predicted polypeptide DNA65410-1569 contains a single open reading frame with an apparent translational initiation site at nucleotide molecular weight of about 17,068 daltons, a pl of about 7.29, and a potential N-glycosylation site at about antinu

5 BAR1_RAT, AF020281_1, HSU95213_1, TCH3_ARATH, LEY14765_1, CATR_NAEGR, S35185, and also shown between the PRO1306 amino acid sequence and the following Dayhoff sequences: JC4902 homology between the PRO1306 amino acid sequence and Dayhoff sequence AIFI_HUMAN. Homology was aligument analysis of the full-length sequence shown in Figure 110 (SEQ ID NO:196), revealed significant An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

deposit no. 203231 Clone DNA65410-1569, was deposited with the ATCC on September 15, 1998 and is assigned ATCC

EXAMPLE 59: Isolation of cDNA clones, Encoding Human PRO1336

- 15 translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) blasted against various EST databases. The EST databases included public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEO*, Incyte Pharmaceuticals, Palo Alto, CA), and proprietary ESTs from Methods in Encymology, 266:460-480 (1996)] as a comparison of the ECD protein sequences to a 6 frame Genericch. The search was performed using the computer program BLAST or BLAST2 [Alischul et al. An EST sequence was identified and emered into a proprietary Generatech database. The EST was
- 20 or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Scattle, Washington).
- ટડ DNA43319 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence (forming an assembly) using phrap. This consensus sequence is designated herein "DNA43319". Based on the A consensus DNA sequence encoding PRO1336 was assembled relative to other aligned EST sequences

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'ATGGAGATTCCTGCCAACTTGCCG3' (SEQ ID NO:199); and

30 TEXESSE PCR primer 5"TTGTTGGCATTGAGGAGGAGCAGC3". (SEQ ID NO:200)

DNA43319 sequence which had the following nucleotide sequence: <u>hybtklization_probe_</u> 5'GAGGGCATCGTCGAAATACGCCTAGAACAGAACTCCATCAAAGCCATCCC3 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus

ß In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

isolate clones encoding the PRO1336 gene using the probe oligonaxteoxide and one of the PCR primers. RNA screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to

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for construction of the cDNA libraries was isolated from human fetal lung tissue

PRO1336 (designated herein as DNA65423-1595 [Figures 111A-B, SEQ ID NO:198]; and the derived protein DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

DNA65423-1595 contains a single open reading frame with an apparent translational initiation site at nucleotide and N-glycosylation sites are indicated in Figure 112. Clone DNA65423-1595 has been deposited with the leucine zipper pattern region, a region conserved in immunoglobulins and major histocompatibility complexes 1-27), aspartic acid and asparagine hydroxylation sites, EGF-like domain cystein pattern signature regions, a polypeptide precursor is 1523 antino acids long. The approximate locations of the signal peptide (amino acids positions 83-85 and an apparent stop codon at nucleotide positions 4652-4654 of SEQ ID NO:198. The predicted The entire coding sequence of PRO1336 is shown in Figures 111A-B (SEQ ID NO:198). Close

5 an estimated molecular weight of about 167.715 daltuns and a pl of about 8.06. ATCC and is assigned ATCC deposit no. 203227. The full-length PRO1336 protein shown in Figure 112 has An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

2 between the PRO1336 amino acid sequence and the following Dayhoff sequences (data incorporated herein) SLIT_DROME, CEF40E10_1, LCU58977_1, AF029779_1, FBP1_STRPU, NOTC_XENLA, AC004663_1 alignment analysis of the full-length sequence shown in Figure 112 (SEQID NO:198), revealed sequence identity XELXDEL_1, P_W05835 and HSU77720_1.

EXAMPLE 60: Isolation of cDNA clones Encodine Human PRO1278

- 20 symbesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is in Example 1 above. This consensus sequence is designated herein "Consen5230". In addition, the Consen5230 designated herein as "DNA44801". Based on the DNA44801 consensus sequence, oligonucleotides were consensus sequence was extended using repeated cycles of BLAST and phrap to extend the consensus sequence A consensus DNA sequence was assembled relative to other EST sequences using phrap as described
- ß probes to isolate a clone of the full-length coding sequence for PRO1278

PCR primers (forward and reverse) were synthesized:

- 30 reverse PCR_primers: CCAGTCGGACAGGTCTCTCCCCTC (44801.r1; SEQ ID NO.206) and forward PCR_primers: GCAGGCTTTGAGGATGAAGGCTGC (44801.f1; SEQ ID NO:204) and CTCATTGGCTGCCTGGTCACAGGC (44801.22; SEQ ID NO:205)
- TCAGTGACCAAGGCTGAGCAGGCG (44801.r2; SEQ ID NO:207) Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus
- DNA44801 sequence which had the following nucleotide sequence:
- 35 SEQ ID NO:208) hybridization.probe; CTACACTCGTTGCAAACTGGCAAAAATATTCTCGAGGGCTGGCCTGQ44801.p1;

screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

isolate clones encoding the PRO1278 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human testis.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1278 (designated herein as DNA66304-1546 [Figure 113, SEQ ID NO:202]; and the derived protein sequence for PRO1278.

The entire coding sequence of PRO1278 is shown in Figure 113 (SEQ ID NO:202). Clone DNA663041546 contains a single open reading frame with an apparent translational initiation site at macleotide positions
141-143 and an apparent stop codon at nucleotide positions 585-587. The predicted polyecptide precursor is 148
amino acids long. The full-length PRO1278 protein shown in Figure 114 has an estimated molecular weight of
about 16,623 datons and a pl of about 8.47. Additional features include a signal peptide sequence at about
amino acids 1-19; a potential N-glycosylation site at about amino acids 58-61; an alpha-lactalbumin/lycozyme
C signature at about amino acids 94-112; and homolgy with alpha-lactalbumin/lycozyme C at about smino acids
35-59, 67-59 and 112-133.

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An analysis of the Dayhoff database (version 33.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 114 (SEQ ID NO:203), revealed significant boundlogy between the PRO1278 amino acid sequence and the following Dayhoff sequences: LYCI_ANAPL, LYC3_ANAPL, and LYC_HUMAN.

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Clone DNA66304-1546 was deposited with the ATCC on October 6, 1998, and is assigned ATCC toposit no. 203321.

20 EXAMPLE 61: Isolation of cDNA clones Encoding Human PRO1298

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from an incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LiFESEQ*, incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a diseased prostate tissue library. The homology search was performed using the computer program BLAST or BLAST2 (Altabul et al., Methods in Enzymology 266:460-480 (1996)) Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56389.

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In light of the sequence homology between the DNAS6389 sequence and an EST sequence contained within an Incyne EST within the assembly from with the consensus sequence was derived, Incyne clone 3355717 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 115 and is herein designated as DNA66511-1563.

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The full length clone shown in Figure 115 contained a single open reading frame with an apparent translational imitation site at nucleotide positions 94-96 and ending at the trop codon found at nucleotide positions 1063-1065 (Figure 115: SEQ ID NO:209). The predicted polypeptide precursor (Figure 116: SEQ ID NO:210)

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is 323 amino acids long. The signal peptide is at about amino acids 1-15 of SEQ ID NO:210. PRO1298 has a calculated molecular weight of approximately 37,017 dahons and an estimated pil of approximately 8.83. Gone DNA66511-1563 was deposited with the ATCC on September 15, 1998 and is assigned ATCC deposit no. 203228.

An analysis of the Dayhoff database (version 35.45 SwissFrot 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 116 (SEQ ID NO:210), revealed sequence identity between the PRO1298 anino acid sequence and the following Dayhoff sequences (data incorporated herein): ALG2_YEAST, CAPM_STAAU, C69098, C69255, SUS2_MATZE, A69141, S74778, AB009527_13, AF050103_2 and BBA224769_1.

EXAMPLE 62: Isolation of cDNA cloucs Encoding Human PRO1301

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte Cluster No. 93492, also referred herein as "DNA10591". This EST cluster sequence was then compared to a variety of expressed sequence to age (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA databases (LIFESEQ®, Incyte Fharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was

15 (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLASTZ (Altahul et al., Methods in Enzymology, 266:460 480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was derived from a CDNA library constructed from RNA isolated from lung tissue removed from a male with adenocarcinoma. The

In light of the sequence homology between the DNA57725 sequence and an EST sequence contained within the EST no. 3395984, the EST clone 3395984 was purchased and the cDNA insert was obtained and sequenced in its entirety. The sequence of this cDNA insert is shown in Figure 117 and is herein designated as 25 "DNA66512-1564".

consensus sequence obtained therefrom is herein designated "DNA57725"

The full length close shown in Figure 117 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 43 to 45 and ending at the stop codon found at nucleotide positiona 1429 to 1431 (Figure 117; SEQ ID NO:211). The predicted polypeptide precursor (Figure 118, SEQ ID NO:211) is 462 amino acids long. Other features of the PRO1301 protein include: a signal sequence at about

- 30 amino acids 1-18; a transmembrane domain at about amino acids 271-290; a cytochrome P450 homologous region at about amino acids 134-462; and potential N-glycosylation sites at about amino acids 94-97, 217-220, and 246-249. PRO1301 has a calculated molecular weight of approximately 52,432 daltons and an estimated p1 of approximately 6.14. Clone DNA66512-1564 was deposited with the ATCC on September 15, 1998 and is assigned ATCC deposit no. 203218.
- 35
 An analysis of the Dayhoff database (version 35.45 SwissProx 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 118 (SEQ ID NO:212), revealed some homology between the PRO1301 amino acid sequence and the following Dayhoff sequences: PSU29243_1, A69975.

ATACC0448418, D78607_1, CEB0331_1, HUMCYTIIIA_1, AF014800_1, CELT13C5_4, CELC45I14_14,

EXAMPLE 63: Isolation of cDNA clones Encoding Human PRO 1268

5 S of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a cluster sequence from the LIFESEQ® database, designated EST No. 8879. This EST cluster sequence was then tissue taken from a cerebral meninges lesion. The concensus requence obtained therefrom is herein designated (Altshul et al., Methods in Enzymology, 266:460-480 (1996)). Those comparisons resulting in a BLAST score existing homologies. The homology search was performed using the computer program BLAST or BLAST? Washington). One or more of the ESTs was derived from a cDNA library constructed from human brain tumor consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Senttle, GenBank) and a proprietary EST DNA database (LIFESEQ®, arcyte Pharmaceuticals, Palo Alto, CA) to identify compared to a varicty of expressed sequence tag (EST) dataleases which included public EST databases (e.g. Use of the signal sequence algorithm described in Example 3 above allowed identification of an ESI

and sequenced. The sequence of this cDNA insert is shown in Figure 119 and is herein designated as within the incyce EST no. 2944541, EST clone no. 2944541 was purchased and the cDNA insert was obtained In light of the sequence hornology between the DNA56258 sequence and an EST sequence contained

20 translational initiation site at nucleotide positions 89 to 91 and ending at the stop codon found at nucleotide N-glycosylation site at about amino acids 79-82, and a region having homology with G-protein coupbled ID NO:214) is 140 amino acids long. PRO1268 has a calculated molecular weight of approximately 15,503 receptors at about amino acids 59-99, positions 509 to 511 (Figure 119; SEQ ID NO:213). The predicted polypeptide precursor (Figure 120, SEQ nt about amino acids 12-28; type I transmembrane domains at thout amino acids 51-66 and 107-124; a potential daltons and an estimated pl of approximately 6.44. Additional features include a type II transmembrane domain The full length clone shown in Figure 119 contained a single open reading frame with an apparent

sequence identity was determined to not be significant. between the PRO1268 amino acid sequence and Dayhoff sequence no. CEF39B2_9. However, the percent alignment analysis of the full-length sequence shown in Figure 120 (SEQ ID NO:214), revealed some homology An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

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Clune DNA66519-1535 was deposited with the ATCC on September 15, 1998 and is assigned ATCC

EXAMPLE 64: Isolation of cDNA clones Encoding Human PRO1269

35 cluster sequence from the LIFESEQ® database, designated EST Cluster No. 101920. This EST cluster sequence was then compared to a variety of expressed sequence tag (ESI) databases which included public EST databases Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

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Seaule, Washington). The consensus sequence obtained therefrom is herein designated DNA56509. BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and BLAST2 (Altabul et al., Methods in Enzymology, 266:460-480 (1996)). Those comparisons resulting in a identify existing homologies. The homology search was performed using the computer program BLAST or (c.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyce Pharmaceuticals, Palo Alto, CA) to assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington,

sequenced. The sequence of this cDNA insert is shown in Figure 121 and is herein designated as DNA66520within the EST no. 103157, EST clone no.103157 was purchased and the cDNA insert was obtained and In light of the sequence homology between the DNAS6509 sequence and an EST sequence contained

15 5 21,731 daltons and an estimated pl of approximately 8.97. 614-616 (Figure 121; SEQ ID NO:215). The predicted polypeptide precursor (Figure 122, SEQ ID NO:216) glycosylation site at about amino acids 112-115. PRO1269 has a calculated molecular weight of approximately is 196 amino acids long, with a signal popiide located at about amino acids 1-20. There is a potential Ntranslational initiation site at nucleoside positions 26-29 and ending at the stop codon found at nucleotide positions The full length close shown in Figure 121 contained a single open reading frame with an apparent

P_W23722. In addition, sequence homology was found between the PRO1269 amino acid sequences and the alignment analysis of the full-length sequence shown in Figure 122 (SEQ ID NO:216), revealed significant homology between the PRO1269 amino acid sequence and the amino acid sequence of Dayhoff sequence no. An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

20 \$75616_1, and NCP_PIG. amino acid sequences of the following Dayhoff sequences: MMTAG7_1, MTV026_16, NAAA_BPT3

deposit no. 203226. Clone DNA66520-1536 was deposited with the ATCC on September 15, 1998, and is assigned ATCC

25 EXAMPLE 65: Isolation of cDNA clones Encoding Human PRQ1327

databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ*, Incyte Pharmaceuticals, Palo Alto sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST cluster sequence from the Incyte database, designated incyte EST cluster sequence no. 173410. This EST cluster Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

- မ CA) to identify existing homologics. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a Scaule, Washington). The consensus sequence obtained therefrom is herein designated DNA56520. assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and
- 35 was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 123 and is herein designated within the Incyte EST clone no. 3451760, the Incyte EST clone no. 3451760 was purchased and the cDNA inser In light of the sequence homology between the DNA56520 sequence and an EST sequence contained

as DNA66521-1583.

Clone DNA66521-1583 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 55-57 and ending at the stop codon at nucleotide positions 811-813 (Figure 123). The predicated polypeptide precursor is 252 amino acids long (Figure 124). The full-length PRO1327 protein shown in Figure 124 has an estimated molecular weight of about 28,127 daltons and a pl of about 8.91. Analysis of the full-length PRO1327 sequence shown in Figure 124 (SEQ ID NO:218) evidences the presence of the following: a signal peptide from about amino acid 10 about amino acid 14, potential N-glycosylation sites from about amino acid 62 to about amino acid 65, from about amino acid 127 to about amino acid 130, from about amino acid 137 to about amino acid 146 and a 2-0x0 acid dehydrogenase acyltransferase homology block from about amino acid 61 to about amino acid 71. Clone DNA66521-1583 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no.

An analysis of the Dayboff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 124 (SEQ ID NO:218), evidenced significant bomology between the PRO1327 amino acid sequence and the following Dayboff sequences: NPH1_RAT, NPH2_MOUSE. OTU_DROME. D40750, BB61_RABIT, P_R23873, P_W09643, CAGHMGPA_1, HUMPRPI1_1 and \$670958_1.

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EXAMPLE 66: Isolation of cDNA clones, Encoding Human PRO1382

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Using the method described in Example 1 above, Incycle EST no. 2719 was identified as a sequence of interest baving a BLAST score of 70 or greater that does not encode a known protein. The nucleotide sequence of EST no. 2719 is designated herein "DNA42842". Based on the DNA42842 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that comtained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1382.

PCR primers (forward and reverse) were synthesized:

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forward PCR primer ACGGCTCACCATGGGCTCCG (42842.fl; SEQ ID NO:221)

TEVELSE PCR primet AGGAAGAGGAGCCCCTTGGAGTCCG (42842.rl; SEQ ID NO:222)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA42842 sequence which had the following nucleotide sequence:

hybridization probe: CGTGCTGGAGGGCAAGTGTCTGGTGGTGTGCGACTCGAAC (42842.pl; SEQ ID 30 NO:223).

lo order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO 1382 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from a human breast carcinoma.

35 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1382 (designated herein as DNA66526-1616 [Figure 125, SEQ 1D NO:219]; and the derived protein sequence for PRO1382.

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The entire coding sequence of PRO1382 is shown in Figure 125 (SEQ ID NO:219). Clone DNA66526-1616 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 337-339 and an apparent stop codon at nucleotide positions 940-942. The predicted polypeptide precursor is 201 amino acids long. The full-length PRO1382 protein shown in Figure 126 has an estimated molecular weight of about 21,808 dations and a pl of about 9.04. Additional features include a signal peptide at about amino acids 1-27; potential N-glycosylation sites at about amino acids 29-32 and 88-91; and regions of homology with C1q proteins at about amino acids 92-126, 159-178, and 191-200.

Au analysis of the Dayhoff datahase (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 126 (SEQ ID NO:220), revealed significant homology between the PRO1382 amino acid sequence Dayhoff sequence no. CERL_RAT. Homology was also 10 revealed between the PRO1382 amino acid sequence and the following Dayhoff sequences: CERB_HUMAN, S76975_1, A41752, HUMCIQB2_1, A57131, CA1A_HUMAN, ACR3_MOUSE, and COLE_LEPMA.

Clone DNA66526-1616 has been deposited with ATCC and is assigned ATCC deposit no. 203246.

EXAMPLE 67: Isolation of cDNA clones Encoding Human PRO1328

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 40671. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a preprietary EST DNA database (Lifeseq®, Incyto Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST 20 or BLAST (Alishul et al., Methods in Enzymology 266:480-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and

BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56749.

In light of the sequence homology between the DNA56749 sequence and an ESI sequence contained.

25 within the Incyte EST clame no. 4111192, the Incyte EST clone no. 4111192 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 127 and is herein designance as DNA66658-1584.

Clone DNA66658-1584 contains a single open reading frame with an apparent translational initiation slie at nucleotide positions 9-11 and ending at the stop codon at nucleotide positions 780-782 (Figure 127). The 30 predicted polyticpide precursor is 257 amino acids long (Figure 128). The full-length PRO1328 protein shown in Figure 128 has an estimated molecular weight of about 28,472 daltons and a pl of about 9.33. Analysis of the full-length PRO1328 sequence shown in Figure 128 (SEQ ID NO.225) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, transmembrane domains from about amino acid 32 to about amino acid 51, from about amino acid 110 to about amino acid 235, a glycosaminoglycan attackment site from about amino acid 120 to about amino acid 25. (Tom about amino acid 25. (Tom about amino acid 25. (Tom about amino acid 26. Clone DNA66658-1584 has family protein homology block from about amino acid 31 to about amino acid 65. Clone DNA66658-1584 has

been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203229.

An analysis of the Dayhoff danbase (version 35.45 SwissProt 35), using a WU-BLAST2 acquence aligument analysis of the full-length sequence shown in Figure 128 (SEQ ID NO:225), evidenced significant homology between the PRO1328 amino acid sequence and the following Dayhoff sequences: CEYF36H2L_2, TIP2_TOBAC, AB009466_16, ATU39485_1, P_R60153, P_R77082, S73351, C69392, LEU95008_1 and FEAAGCT

EXAMPLE 68: Isolation of cDNA clones Encoding Human PRO1325

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the lineyte database, designated Incyte EST cluster sequence no. 139524. This EST cluster sequence was then compared to a variety of expressed sequence to ag (EST) databases which included public EST databases (Lifeseq*, Incyte Pharmaccuicals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 256:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Searde, Washington). The consensus sequence with the program is herein designated DNAS6115.

In light of the sequence homology between the DNA56115 sequence and an EST sequence contained within the Incyte EST clone no. 3744079, the Incyte EST clone no. 3744079 was purchasted and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 129 and is herein designated as DNA66659, 1593

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ઝ မွ 25 amino acid position 496 to about amino acid position 499, from about amino acid position 572 to about amino 518 and potential N-glycosylation sites from about amino acid 27 to about amino acid 30, from about amino acid of the full-length PRO1325 sequence shown in Figure 130 (SEQ ID NO:227) evidences the presence of the acid position 699 to about amino acid position 702. Clone DNA66659-1593 has been deposited with ATCC on 123 to about amino acid position 126, from about amino acid position 141 to about amino acid position 144, 54 to about amino acid 57, from about amino acid 60 to about amino acid 63, from about amino acid position acid position 575, from about amino acid position 603 to about amino acid position 606 and from about amino from about amino acid position 165 to about amino acid position 168, from about amino acid position 364 to 751 to about amino acid 770, a leucine zipper pattern sequence from about amino acid 497 to about amino acid acid 501 to about amino acid 520, from about amino acid 607 to about amino acid 627 from about amino acid following: a signal peptide from about amino acid 1 to about amino acid 18, transmembrane domains from about shown in Figure 130 has an estimated molecular weight of about 94,454 daltons and a pl of about 6.94. Analysis The predicted polypeptide precursor is 832 amino acids long (Figure 130). The full-length PRO1325 procein about amino acid position 367, from about amino acid position 476 to about amino acid position 479, from about amino acid 292 to about amino acid 317, from about amino acid 451 to about amino acid 470, from about amino site at nucleoride positions \$1-53 and ending at the stop codon at nucleoride positions 2547-2549 (Figure 129) Clone DNA66659-1593 contains a single open reading frame with an apparent translational initiation

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September 22, 1998 and is assigned ATCC deposit no. 203269.

An analysis of the Dayhoff database (version 35.45 SwissProx 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 130 (SEQ ID NO:227), evidenced significant homology between the PRO1325 smino acid sequence and the following Dayhoff sequences: CELROHES_1, CELZK721_5, CELC30EI_5, CELC30EI_6, CELC30EI_2, CEY37H2C_1, CELC30EI_7, CELT07H8_7 and E64006.

EXAMPLE 69: Isolation of cDNA clones Encoding Human PRO 1340

Using the method set forth in Example 1 above, Incyre EST no. 878906 was identified as a sequence of interest having a BLAST score of 70 or greater that does not encode a known protein. The nucleotide 10 sequence of EST no. 878906 is designated herein "DNA42809". Based on the DNA42809 sequence.

PCR primers (forward and reverse) were synthesized:

and 2) for use as probes to isolate a clone of the full-length coding sequence tor PRO1340

oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that comained the sequence of interest

forward PCR primer TCCAGGTGGACCCCCACTTCAGG (42809.f1; SEQ ID NO:270)

reverse PCR primer GGGAGGCTTATAGGCCCCAATCTGG (42809:1; SEQ ID NO:271)

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Additionally. a symbetic oligonucleoside hybridization probe was constructed from the DNA42809 sequence which had the following nucleoside sequence:

https://dization_prote_GGCTTCAGCAGCACGTGTGAAGTCGAAGTCGCAGTCACAGATATCAATGA_(42809.p1; SEQ ID NO:272)

20 In order to screen several libraries for a source of a full-length clone. DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1340 gene using the probe oligonucleoide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1340 (destignated horein as DNA66663-1598 [Figure 131, SEQ ID NO:228]; and the derived protein sequence for PRO1340.

The entire coding sequence of PRO1340 is shown in Figure 131 (SEQ ID NO:228). Close DNA666631598 contains a single open reading frame with an apparent translational initiation site at nucleoside positions
128-130 and an apparent stap codon at nucleotide positions 2549-2551. The predicted polypeptide precursor
30 is 807 amino acids long. The full-length PRO1340 protein shown in Figure 132 has an estimated molecular
weight of about 87,614 dations and a pl of about 4.83. Additional features include: a signal peptide at about
amino acids 1-18; a transmembrane domain at about amino acids 762-784; a cell attachment sequence at about

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An analysis of the Dayhoff database (version 33.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 132 (SEQ ID NO:229), revealed significant homology between the PRO1340 amino acid sequence and Dayhoff sequence no. 146536. Homology was also

cadherin extracellular repeat domains at about amino acids 307-351, 324-348, 67-103, 97-141 and 114-138.

amino acids 492-494; potential N-glycosylation sites at about amino acids 517-520, 602-605 and 700-703; and

revealed between the PRO1340 amino acid sequence and the following Dayhoff sequences: S55396, RATPDRPT_I, CADD_CHICK, CAD1_CHICK, CAD8_CHICK, ISO180, CAD4_CHICK, G02878, and DSC1_MOUSE.

Clone DNA66663-1598 has been deposited with ATCC and is assigned ATCC deposit no. 203268.

EXAMPLE 70: Isolation of cDNA clones Encoding Human PRO1339

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This convensus sequence is designated herein "DNA40632". Within the consensus sequence assembly was heave EST 2479394. Based on the consensus sequence and other discoveries and information provided herein, the clone including lacyte EST 2479394 was purchased and sequenced in full. Sequencing provided the meleic acid sequence shown in Figure 133 which includes the sequence encoding PRO1339.

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Clone DNA66669-1397 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 9-11 and an apparent stop codon at nucleotide positions 1272-1274 of SEQ ID NO:233. The predicted polypeptide precursor is 421 amino acids long. The signal peptide is at about amino acids 1-16 of SEQ ID NO:234. The region conserved in zinc carboxypeptidases and the N-glycosylation site are indicated in Figure 134. Clone DNA66669-1597 has been deposited with the ATCC and it assigned ATCC deposit no. 203272. The full-length PRO1339 protein shown in Figure 134 has an estimated molecular weight of about 47,351 dations and a p1 of about 6,61.

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An analysis of the Dayboff database (version 35.45 SwitsProt 35), using a WU-BLAST2 sequence 20 alignment analysis of the full-length requence shown in Figure 134 (SEQ ID NO.234), revealed sequence identity between the PRO1339 amino acid sequence and the following Dayboff sequences (data incorporated herein): P_W01505, CBP1_IIUMAN, HSA224866_1, P_R90293, YHT2_YEAST, CEF02D8_4, CEW01A8_6, P_W36815, HSU83411_1 and CBPN_HUMAN.

25 EXAMPLE 71: Isolation of cDNA clones Encoding Human PRO1337.

Using the method described in Example 1 above, a single heyre EST was identified (EST No. 1747546) and also referred to herein as "DNA4417". To assemble a consensus sequence, repeated cycles of BLAST and phrap were used to extend the DNA4417 sequence as far as possible using the sources of EST sequences discussed above. The consensus sequence is designated herein as "DNA45669". Based on the DNA45669 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for

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PCR primers (forward and reverse) were synthesized:

55 CTTTGCTGTTGGCCTCTGTGCTCCCAACGACAGGCCAGG (45669.1; SEQ ID NO:237) and CTTTGCTGTTGGCCTCTGTGCTCCCAACGATGCAAGGACAGGCCAGG (45669.1; SEQ ID NO:238); EXERSE PCR primers: TGACTCGGGGTCTCCAAAACCAGC (45669.1; SEQ ID NO:239) and GGTATAGGCGGAAGGCAAAGTCGG (45669.2; SEQ ID NO:240);

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Additionally, a synthetic oligonacleotide hybridization probe was constructed from the consensus DNA45669 sequence which had the following nucleotide sequence:

hthidizai@nproles: GGCATCTTACCTTTATGGAGTACTCTTTGCTGTTGGCCCTCTGTGCTCC(45569,pt; SFQ ID NO:241).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1337 gene using the probe oligonacleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1337 (designated herein as DNA66672-1586 [Figure 135, SEQ ID NO:235]; and the derived protein sequence for PRO1337.

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The entire coding sequence of PRO1337 is shown in Figure 135 (SEQ ID NO:235). Clone DNA66672-1586 contains a single open reading frame with an apparent translational initiation site at mucleotide positions 60-62 and an apparent stop codon at nucleotide positions 1311-1313. The predicted polypeptide precursor is 417 amino actids long. The full-length PRO1337 protein shown in Figure 136 has an estimated molecular weight of about 46.493 daitons and a pl of about 9.79.

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An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 136 (SEQ ID NO:236) revealed significant boundogy between the PRO1337 amino acid sequence and the Dayhoff sequence THBQ_HUMAN. Homology was also found between the PRO1337 amino acid sequence and the following Dayhoff sequences as the following Dayhoff sequences.

KAIN_HUMAN, HSACTI_1.1F8P_HUMAN, G02081, HAMHPP_1, CP16_RAT. S31507, AB000547_1, and

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KBP_MOUSE.

Clone DNA66672-1586 was deposited with the ATCC on September 22, 1998, and is assigned ATCC deposit no. 203265.

25 EXAMPLE 72: Isolation of cDNA clones Encoding Human PRO1342

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA43203. The DNA43203 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and proprietary EST DNA databases (LTESEQTM, Incyte Pharmaceruticals, Palo Alto, CA; Genentech, South San Francisco, CA) to identify existing homologics. The homology starch was performed using the computer program BLAST or BLAST2

- 30 existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology, 265:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is designated herein as "DNA48360".
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 Based on the DNA48360 requence, oligonucleotide probes were generated and used to screen a human esophageal tissue library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRKSB (pRKSB is a precursor of pRKSD that does not contain the Sfil site: see, Holmes et al., Science,

253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

reverse PCR primer: 5'- GTCAGAGTTGGTTGGTTGCTAGC-3' (48360.rl; SEQ ID NO:245) forward PCR primer: 5'-GAAGCACCAGCCTTTATCTCTTCACC-3' (48360.f1; SEQ ID NO:244)

which had the following nucleotide sequence: Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA48360 sequence

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5'GGACCCAGGCATCTTGCTTTCCAGCCACAAAGAGACAGATGAAGATGC-3 (48360.p1; SEQ

screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1342 gene using the probe oligonucleotide and one of the PCR primers. In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

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molecular weight of approximately 57, 173 daltons and an estimated pl of approximately 4.82. Additional features 307, 359-412, 194-247, 239-292, 299-352, 134-187, 314-367, and 164-217. acids 325-328; and bacterial ice-nucleation protein octamer repeats at about amino acids 284-337, 404-457, 254 include: signal sequence at about amino acids 1-20; a transmembrane domain at about amino acids 510-532; a (Figure 137; SEQ ID NO:242). The predicted polypeptide precursor is 596 amino acids long has a calculated translational initiation site at nucleotide positions 239-241, and a stop signal at nucleotide positions 2027-2029 potential N-glycosylation site at about amino acids 25-28; a glycosaminoglycan attachment site at about amino A full length clone was identified that contained a single open reading frame with an apparent

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CELKO6A9_3, and YM96_YEAST. LMSAP2GN_I, D88734_, AMYH_YEAST, MMDSPPG_1, VGLX_HSVEB, S52714, CELF59A6_5, homology between the PRO1342 amino acid sequence and the following Dayhoff sequences: CELZC178_2, alignment analysis of the full-length sequence shown in Figure 138 (SEQ ID NO:243), evidenced some An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

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23 deposit no. 203281. Clone DNA66674-1599 was deposited with the ATCC on September 22, 1998, and is assigned ATCC

EXAMPLE 73: Isolation of cDNA clones Encoding Human PRO1343

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BLAST2 sequence alignment computer program, to have no significant sequence identity to any known human encoding nucleic acid. This cDNA sequence is herein designated DNA48921. Probes were generated from the as described in paragraph 1 above. The cloning vector was pRKSB (pRKSB is a precursor of pRKSD that does sequence of the DNA48921 molecule and used to screen a human smooth muscle cell tissue library prepared not contain the Sfil site; see, Holmes et al., <u>Science, 253</u>:1278-1280 (1991)), and the cDNA size cut was less A cDNA sequence isolated in the amylase screen described in Example 2 above was found, by the WU

The oligonucleotide probes employed were as follows:

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forward PCR primes (48921.f1) 5'-CAATATGCATCTTGCACGTCTGG-3' (SEQ ID NO:249)

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hybridization probe (48921.p1) REVELUE PCR PRIMEE (48921.rl) 5'-AAGCTTCTCTGCTTCCTTTCCTGC-3' (SEQ ID NO:250)

5'-TGACCCCATTGAGAAGGTCATTGAAGGGATCAACCGAGGGCTG-3' (SEQ ID NO:251)

10 September 22, 1998 and is assigned ATCC deposit no. 203282. 139, SEQ ID NO:247). The predicted polypeptide precursor is 247 amino acids long, has a calculated molecular peptide from about amino acid 1 to about amino acid 25 and a homologous region to circumsporozoite repeats translational initiation site at nucleotide positions 71-73 and a stop signal at nucleotide positions 812-814 (Figure PRO1343 sequence shown in Figure 140 (SBQ ID NO:248) evidences the presence of the following: a signal weight of approximately 25,335 dalums and an estimated pl of approximately 7.0. Analysis of the full-length from about amino acid 35 to about amino acid 225: Clone DNA66675-1587 has been deposited with ATCC on A full length clone was identified that contained a single open reading frame with an apparent

HUMPROFILE_1 and MTV023_14. CEF25H8_2, U88974_40, BNAMRNAA_1, BOBOPC3_1, S58135, AF061832_1, BHU52040_1 alignment analysis of the full-length sequence shown in Figure 140 (SEQ ID NO:248), evidenced significam homology between the PRO1343 amino acid sequence and the following Dayhoff sequences: CSP_PLACC, An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

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sequence was obtained and the insert sequenced, thereby giving rise to the DNA66675-1587 sequence shown Additionally, an Incyte EST clone (Incyte EST clone no. 4701148) having homology to the DNA48921

8 EXAMPLE 74: Isolation of cDNA clones Encoding Human PRO1480

University of Washington, Seattle, Washington). This consensus sequence is designated herein as "DNA 1395". sequences were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green as sequences of interest having BLAST scores of 70 or greater that did not encode known proteins. These Using the methods described in Example 1 above, Incyte EST Nos. 550415 and 1628847 were identified

8 z In addition, the "DNA 1395" consensus sequence was extended using repeated cycles of BLAST and phrap to of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1480. sequence, oligonucleotides were symbesized: 1) to identify by PCR a cDNA library that contained the sequence extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is designated herein as "DNA40642". Based on the DNA40642 consensus

PCR primers (forward and reverse) were synthesized:

forward PCR primer: AGCCCGTGCAGAATCTGCTCCTGG (40642.f1; SEQ ID NO:254)

GTACAGGCTGCAGTTGGC (40642.r2; SEQ ID NO:256) EXPLISE PCR primers: TGAAGCCAGGGCAGCGTCCTCTGG (40642.r1; SEQ ID NO:255);

ß DNA40642 sequence which had the following nucleotide sequence: Additionally, synthetic oligonucleotide hybridization probes were constructed from the consensus

NO:257); GAGCTGCAGATCTTCTCATCGGGACAGCCCGTGCAGAATCTGCTC (40642.p2; SEQ ID <u>hybridization.proben</u>: AGAAGCCATGTGAGCAAGTCCAGTTCCAGCCCAACACAGTG(40642.p1; SEQ ID

VO:258).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1480 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-longth DNA sequence for PRO1480, designated herein as DNA67962-1649 [Figure 141, SEQ ID NO:252]; and the derived protein sequence for PRO1480.

The entire coding sequence of PRO1480 is shown in Figure 141 (SEQ ID NO:253). Clone DNA67962-1649 contains a single open reading frame with an apparent translational initiation site at mucleotide positions 10 241-243 and an apparent stop codon at nucleotide positions 2752-2754. The predicted polypeptide precursor is 837 amino acids long. The bull-length PRO1480 protein shown in Figure 142 has an estimated molecular weight of about 92,750 dations and a pl of about 7.04. Additional features the bude: transmembrane domains at about amino acids 23-46 (type II) and 718-738; potential N-glycosylation sites at about amino acids 69-72, 96-99.

An analysis of the Dayhoff database (version 35.45 SwitsProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 142 (SEQ ID NO:233), revealed significant homology between the PRO1480 amino acid sequence and Dayhoff sequence 148746. Homology was also shown between the PRO1480 amino acid sequence and the following Dayhoff sequences: S66498; P_W17658; MMU69335_1; HSU60800_1; 48745; A49069; M8747; GGU28240_1; and AF022946_1.

165-168, 410-413, 525-528, and 630-633; and a leucine zipper pattern at about amino acids 12-33.

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Clone DNA67962-1649 has been deposited with ATCC and is assigned ATCC deposit no. 203291.

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EXAMPLE 75: Isolation of cDNA clones Encoding Human PRO1487

A single Merck EST, HSC2ID011, referred herein as "DNA8208", was identified as an EST of interest having a BLAST score of 70 or greater that did not encode a known protein as described in Example 1 above. The DNA8208 sequence was extended using repeated cycles of BLAST and the program "phrap" (Phil Green, University of Washington, Seattle, Washington) to extend the sequence as far as possible using the sources of EST sequences discussed above. The resulting consensus sequence is designated herein as "DNA68836". Based on the DNA68836 consensus sequence, oligonuclootides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1487.

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PCR primers (forward and reverse) were synthesized:

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SCHWARD PCR primer: GTGCCACTACGGGGTGTGGACGAC (54209.11; SEQ ID NO:261) and EXERGE PCR primer TCCCATTTCTTCCGTGGTGCCCAG (54209.11; SEQ ID NO:262)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA68836 sequence which had the following mucheotide sequence:

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hybridization prote CCAGAAGAAGTCCTTCATGATGCTCAAGTACATGCACGACCACTAC (\$4299.p);
SEQ ID NO:263)

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In order to screen several libraries for a source of a full-length clone. DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1487 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated human fetal bidney clasue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1487 (designated herein as DNA68836-1656 (Figures 143A-B; SEQ ID NO:259) and the derived protein sequence for PRO1487 (Figure 144; SEQ ID NO:260).

The entire cuding sequence of PRO1487 is shown in Figures 143A-B (SEQ ID NO:259). Clone DNA68836-1656 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 489-491 and an apparent stop codom at nucleotide positions 2895-2897. The predicted polypeptide precursor is 802 amino acids long. The full-length PRO1487 protein shown in Figure 144 has an estimated molecular weight of about 91,812 dultons and a p1 of about 9.52. Additional features include a signal peptide at about amino acids 1-23; potential N-glycosylation sites at about amino acids 189-192, 623-626, and 796-799; and a octl attachment sequence at about amino acids 62-64.

An analysis of the Dayhoff database (version 35.45 SwissProv 35), using a WU-BLAST2 sequence 15 alignment analysis of the full-length sequence shown in Figure 144 (SEQ ID NO:260), revealed significant homology between the PRO1487 amino acid sequence and the following Dayhoff sequences: CET24D1 1, \$44860, CELC02H6_1, CEC38H2_3, CELC17A2_5, CET09E11_10, CEE03H4_3, CELT72B11_3, GGU82088_1, and CEF56H6_1.

Close DNA68836-1656 was deposited with the ATCC on November 3, 1998, and is assigned ATCC 20 deposit no. 203455.

EXAMPLE 76: Isolation of cDNA ciones Encoding Human PRO1418

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from an Incyce database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a placetta tissue library. The bomology search was performed using the computer program BLAST or BLAST2 (Altabatl et al., Mcthods in Enzymology, 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNAS8445.

In light of the sequence homology between the DNA58845 sequence and an EST included in Incyte clone 1306026, that clone was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 145 and is herein designated as DNA68864-1629.

The full length clone shown in Figure 145 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 138-140 and ending at the stop codon found at nucleotide

positions 1188-1190 (Figure 145; SEQ ID NO:264). The predicted polypeptide precursor (Figure 146, SEQ ID NO:265) is 350 amino acids long with a signal peptide at about amino acids 1-19 of SEQ ID NO:265. PRO1418 has a calculated molecular weight of approximately 39,003 daltons and an estimated pl of approximately 5.59. Clone DNA68864-1629 was deposited with the ATCC on September 22, 1998 and is assigned ATCC deposit no. 203276.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 146 (SEQ ID NO:265), revealed sequence identity between the PRO1418 amino acid sequence and the following Dayhoff sequences (data incorporated herein): AGAI_HAEIN (immunoglobulin al protease precursor), P_W03740, CELT23E7_1, SSN6_YEAST, MNFININ_1, AB00993_1, P_RS2601, S22624, A10377_1 and MUA1_XENLA.

EXAMPLE 77: Isolation of cDNA clones Encoding Human PRO1472

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An Incyte sequence was identified and put in a computer to determine whether it had homology with other proteins in databases. The EST databases included public EST databases (e.g., GenBath), and the proprietary EST databases (LIFESEQ*, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 256:460-480 (1996)] as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green,

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A consensus DNA sequence encoding PRO1472 was assembled relative to other EST sequences using phrap. This consensus sequence is designated herein "DNA62824". Based on the DNA62824 consensus sequence and other discoveries and information provided herein, the Incyte clone including EST 1579843 (from a duodenal bissue library) found in the assembly was purchased and sequenced in full.

University of Washington, Scattle, Washington).

Sequencing provided the entire coding sequence of PRO1472 as shown in Figure 147 (SEQ ID NO:266). Clone DNA68866-1644 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 134-136 and an apparent stop codon at nucleotide positions 1532-1534 of SEQ ID NO:266. The predicted polypeptide precursor is 466 amino acids long. As indicated in Figure 148, the signal peptide is at about amino acid positions 1-17 and the transmembrane domains are at about positions 131-150 and 235-239 of SEQ ID NO:267. Clone DNA68866-1644 has been deposited with ATCC and is assigned ATCC deposit no. 203283. The full-length PRO1472 protein shown in Figure 148 has an estimated molecular weight

An analysis of the Dayboff database (version 35.45 SwitssProt 35), using a WU-BLAS712 sequence alignment analysis of the full-length sequence shown in Figure 148 (SEQ ID NO.267), revealed sequence identify between the PRO1472 amino acid sequence and the following Dayboff sequences (data incorporated herein):

35 BUTY_HUMAN, HS45P21_1, HS45P21_3, HS45P21_5, HS45P21_4, HSU90142_1, HSU90145_1,

AF033107_1, MMHC135G15_7 and HSB73_1.

of about 52,279 daltons and a pl of about 6.16.

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EXAMPLE 78: Isolation of cDNA clones Encoding Human PRQ1461

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated lacyte EST Cluster No. 159103, and also referred to berein as "DNA10747". The DNA10747 sequence was then computed to a variety of EST databases which included public EST databases (e.g., GenBank) and the LIFESEQ® database, to identify existing homologies.

The homology search was performed using the computer program BLAST or BLAST2 (Altabul et al., Method

5 The homology search was performed using the computer program BLAST or BLAST2 (Altabul et al., <u>Method in Enzymology 266</u>:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs used in the assembly was derived from a library constructed from pancreatic tumor tissue. The consensus 10 sequence obtained therefrom is herein designated "DNA59533".

In light of the sequence homology between the DNA59553 sequence and an EST sequence counsined within incyce EST no. 2944541, the EST clone was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 149 and it herein designated as DNA68871-1638.

The full length clone shown in Figure 149 contained a single open reading frame with an apparent 15 translational initiation site at nucleotide positions 32-34 and ending at the stop codon found at nucleotide positions 1301-1303 (Figure 149; SEQ ID NO:268). The predicted polypeptide precursor (Figure 150, SEQ ID NO:269) is 423 amino acids long. PRO1461 has a calculated molecular weight of approximately 47,696 dalums and an estimated pi of approximately 8.96. Additional features include: a type II transmembrate domain at about amino acids 2.1-40; an ATP/GTP-binding site motif A (P-loop) at about amino acids 359-366; a tryptin family histidize

20 active site at about amino acids 228-233; potential N-myristoylation sites at about amino acids 179-184, 213-218, 317-322, and 360-365; and potential N-glycosylation sites at about amino acids 75-78, 166-169 and 223-226.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence.

alignment analysis of the full-length sequence shown in Figure 150 (SEQ ID NO:269), revealed significant bornology between the PRO1461 amino acid sequence Dayhoff sequence no. P. R89435. Homology was also 25 found to exist between the PRO1461 amino acid sequence and the following additional Dayhoff sequences:

AB002134_1, P_R89430, P_W22987, HEPS_MOUSE, ENTK_HUMAN, P_W22986, KAL_MOUSE, ACRO_PIG, p_R57283, and TRYY_ANOGA.

Cione DNA68871-68871 was deposited with the ATCC on September 22, 1998, and it assigned ATCC deposit no. 203280.

EXAMPLE 79: Isolation of cDNA clones Encoding Human PRO1410

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence no. 98502. This EST cluster sequence no. 98502. This EST cluster sequence no. 98502. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., Gembank) and a proprietary EST DNA database (LIFESEQ*, Insyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology, 285:460-480 (1996)). Those comparisons resulting in a

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BLAST score of 70 (or in some cases 90) or greater that did not emonde known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seartle, Washington). The consensus sequence obtained therefrom is herein designated DNAS6451.

In light of the sequence homology between the DNA56451 sequence and an EST sequence contained within the Incyte EST clone no. 1257046, the incyte EST clone 125046 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 151 and is herein designated as

Clone DNA68874-1622 contains a single open reading frame with an apparent translational initiation site at mucleotide positions 152-154 and ending at the stop codon at nucleotide positions 866-868 (Figure 151). The predicted polypeptide practursor is 238 amino acids long (Figure 152). The full-length PRO1410 protein shown in Figure 152 has an estimated molecular weight of about 25,262 dattons and a pl of about 6,44. Analysis of the full-length PRO1410 sequence shown in Figure 152 (SEQ ID NO:271) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 20, a transmembrane domain from about amino acid 194 to about amino acid 220 and a potential N-glycosylation site from about amino acid 135. Clone DNA68874-1622 has been deposited with ATCC on September 22, 1998 and is assigned ATCC deposit no. 203277

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An analysis of the Dayhoff danabase (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 152 (SEQ ID NO:271), evidenced significant homology between the PRO1410 amino acid sequence and the following Dayhoff sequences: I48552, P_R76466, HSMHC3W36A_2, EPB4_HUMAN, P_R14256, EPA8_MOUSE, P_R77285, P_W13569, AFD00560_1, and ASF1_HELAN.

EXAMPLE 80: Isolation of cDNA clones Encoding Human PRO1568

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A consensus DNA sequence was assembled relative to other EST sequences using phrap to form an assembly as described in Example 1 above. The consensus sequence is designated herein "DNA\$4208". Based on the DNA\$4208 consensus sequence, the assembly and other information and discoveries provided herein, a clone including an EST in the assembly was ordered and sequenced. The EST is incyto 3089490. Sequencing in full gave the sequence shown in Figure 153.

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The entire coding sequence of PRO1568 is included in Figure 153 (SEQ ID NO:272). Close DNA68880-1676 contains a single open reading frame with an apparent translational infrintion site at nucleotide 30 positions 208-210 and an apparent stop codon at nucleotide positions 1123-1125 of SEQ ID NO:272. The predicted polypeptide precursor is 305 amino acids long. The signal peptide, transmembrane regions, N-myritoxylation and amidation sites are also indicated in Figure 154. Clone DNA68880-1676 has been deposited with the ATCC and is assigned ATCC deposit no. 203319. The full-length PRO1568 protein shown in Figure 154 has an estimated molecular weight of about 35,383 datlons and a p1 of about 5.99.

An analysis of the Dayhoff database (version 35.45 SwissProx 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 1.54 (SEQ ID NO.273), revealed sequence identity between the PRO1568 amino acid sequence and the following Dayhoff sequences (incorporated herein):

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AR089749_1, AR054941_1, NAG2_HUMAN, CD63_HUMAN, CD82_HUMAN, P_W05732, P_R86814 A15_HUMAN, P_W27333 and CD37_HUMAN.

EXAMPLE 81: Isolation of cDNA clones Encuding Human PRO1570

A consensus DNA sequence encoding PRO1570 was ascembled relative to other EST sequences using phrap as described in Example 1 above to form an assemby. This consensus sequence is designated herein as "DNA65415". Based on the DNA65415 consensus sequence and other discoveries and information provided herein, the clone including Incyte EST 3232285 (from a uterine/colon cancer tissue library) was purchased and sequenced in full which gave SEQ ID NO:274.

The entire coding sequence of PRO1570 is included in Figure 155 (SEQ ID NO:274). Clone 10 DNA68885-1678 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 210-212 and an apparent stop codon at nucleotide positions 1506-1508 of SEQ ID NO:274. The predicted polypeptide procursor is 432 amino acids long. Figure 275 shows a number of mostif. Clone DNA68885-1678 has been deposited with the ATCC and is assigned ATCC deposit no. 203311. The full-tength PRO1570 protein shown in Figure 156 has an estimated molecular weight of about 47,644 daltons and a pl of 15 about 5.18.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 156 (SEQ ID NO:275), revealed sequence identify between the PRO1570 amino acid sequence and the following Dayhoff sequences (incorporated herein): P_W22986, TMS2_HUMAN, HEPS_HUMAN, P_R89435, AB002134_1, KAL_MOUSE, ACRO_HUMAN, GEN12917, AF045649_1, and P_W34285.

EXAMPLE 82: Isolation of cDNA clones Encoding Human PRO1317

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A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "Consen8865". In addition, the Consen8865 25 consensus sequence was extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is designated herein as "DNA63334". Based on the DNA63334 consensus sequence, oligomateleoticles were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1317.

PCR primers (forward and reverse) were synthesized:

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EXPERIENCE: CTGCTGGTGAAATCTGGCGTGGAG (63334.F1; SEQ ID NO:278); and EXPERIENCE: GTCTGGTCCTGGCTGTCCACCCAG (6334.F1; SEQ ID NO:279).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA63334 sequence which had the following nucleotide sequence:

35 http://dizariomprotes: CATCTTGTCATGTACCTGGGAACCACCACAGGGTTCGCTCCACAAQ63334.pl;SEQ ID NO.280).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

for construction of the cDNA libraries was isolated from human hippocampal tissue. isolate clones emooding the PRO1317 gene using the probe oligonucleotide and one of the PCR primers. RNA screened by PCR amplification with the PCR prince pair identified above. A positive library was then used to

PRO1317 (designated herein as DNA71166-1685 [Figure 157, SEQ ID NO:276]; and the derived protein DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

is 761 amino acids long and has an estimated molecular weight of about 83,574 daltons and a pl of about 6.78 105-107 and an apparent stop codon at nucleotide positions 2388-2390. The predicted polypeptide precursor 1685 contains a single upen rending frame with an apparent translational initiation site at nucleotide positions The entire coding sequence of PRO1317 is shown in Figure 157 (SEQ ID NO:276). Clone DNA71166

P_W58540, P_217657, MUSC1_1, P_471380, U73167_5, HSU33920_1, and GG828240_1. revealed between the PRO1317 amino acid sequence the following Dayhoff sequences: 148746, GEN13418, bomology between the PRO1317 amino acid sequence and Dayhoff sequence no. 148745. Homology was also aligament analysis of the full-length sequence shown in Figure 158 (SEQ ID NO:277), revealed significant An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

Clone DNA71166-1685 was deposited with the ATCC on October 20, 1998, and is assigned ATCC

EXAMPLE 83: Isolation of cDNA clones, Encoding Human PRO1780

25 20 repeased cycles of BLAST and the program "phrap" (Phil Green, University of Washington, Seattle) to extend consensus sequence is designated herein as *DNA63837". Based on the DNA63837 consensus sequence, the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1780. oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest The DNA63837.init sequence was obtained as described in Example 1 above and was extended using

PCR primers (forward and reverse) were synthesized:

forward PCR primer: TGCCTTTGCTCACCTACCCCAAGG (63837.11; SEQ ID NO:283) EXYETSE PCR primer: TCAGGCTGGTCTCCAAAGAGAGGGG (63837.11; SEQ ID NO:284)

DNA63837 sequence which had the following nucleotide sequence: Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus

30 hybridization probe: SEQ ID NO:285) CCCAAAGATGTCCACCTGGCTGCAAATGTGAAAATTGTGGACTGG (63837.pl

for construction of the cDNA libraries was isolated from a human fetal kidney. screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clemes encoding the PRO1780 gene using the probe oligonucleotide and one of the PCR primers. RNA In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

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PRO1780 (designated herein as DNA71169-1709 [Figure 159, SEQ ID NO:281]; and the derived protein DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

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sequence for PRO1780

about 59,581 daltons and a pl of about 8.68. Additional features include a signal peptide sequence at about 68-70 and an apparent stop codon at nucleotide positions 1637-1639. The predicted polypeptide precursor is 523 amino acids 68-74 and 425-433; N-myristoylation sites at about amino acids 16-21, 301-206, 370-375, and 494 1709 contains a single open reading frame with an apparent translational initiation site at mucleoxide positions amino acids 1-19; a transmembrane domain at about amino acids 483-504; tyrosine phosphorylation sites at about amino acids long. The full-length PRO1780 protein shown in Figure 160 has an estimated molecular weight of The entire coding sequence of PRO1780 is shown in Figure 159 (SEQ ID NO:281). Clone DNA71169.

5 alignment analysis of the full-length sequence shown in Figure 160 (SEQ ID NO:282), revenled significant CGT_HUMAN, UDI1_HUMAN, P_R26153, UDBI_RAT, HSU59209_1, AB010872_1, UDBS_MOUSE, UDB8_HUMAN, and UD14_HUMAN. homology between the PRO1780 amino acid sequence and the following Dayhoff sequences: UDA2_RABIT An analysis of the Daybolf database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

499; and a leucine zipper pattern at about amino acids 493-514.

deposit no. 203467 Clone DNA71169-1709 was deposited with the ATCC on November 17, 1998, and is assigned ATCC

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EXAMPLE 84: Isolation of cDNA clones Encoding Human PRO1486

20 the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for consensus sequence, oligonucleotides were symbesized: 1) to identify by PCR a cDNA library that contained in Example 1 above. This consensus sequence is designated herein "DNA48897". Based on the DNA48897 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

PCR primers (forward and reverse) were synthesized:

PRO1486.

tenere PCR primer 5'CAGAGAGGGAAGATGAGGAAGCCAGAG3' (SEQ ID NO:289) forward PCR primer 5'AGGCAGCCACCAGCTCTGTGCTAC3' (SEQ ID NO:288); and

25

DNA48897 sequence which had the following nucleotide sequence: Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus

hybridization probe 5'CTGTGCTACTGCCCTTGGACCCTTGGGACCGAGTGTCTCTGC3' (SEQ ID

30 for construction of the cDNA libraries was isolated from a human adenocarcinoma cell line isolate clones encoding the PRO1486 gene using the probe oligonucleotide and one of the PCR primers. RNA screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

PRO1486 and the derived protein sequence for PRO1486 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

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DNA71180-1655 contains a single open reading frame with an apparent translational initiation site at nucleotide The entire coding sequence of PRO1486 is included in Figure 161 (SEQ ID NO:286). Clone

and a pi of about 7.07. The full-length PRO 1486 protein shown in Figure 162 has an estimated molecular weight of about 21,521 daltons 162. Clone DNA71180-1655 has been deposited with the ATCC and is assigned ATCC deposit no. 203403. SEQ ID NO:287. Regions similar to those of Cly and an N-glycosylationi site are located as indicated in Figure predicted polypeptide prectursor is 205 amino acids long. The signal peptide is at about amino acids 1-32 of positions 472-474 and an apparent stop codon at nucleotide positions 1087-1089 of SEQ ID NO:286. The

HUMC1Qb2_1, ACR3_MOUSE CERL_RAT, GEN11893, P_R22263, CA18_HUMAN, CIQC HUMAN, AF054891_1, A57131, between the PRO1486 amino acid sequence and the following Dayhoff sequences: CERB_HUMAN aligument analysis of the full-length sequence shown in Figure 162 (SEQ ID NO:287), revealed sequence identify An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

EXAMPLE 85: Isolation of cDNA clones Encoding Human PRO1433

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5 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for in Example 1 above. This consensus sequence is herein designated DNA45230. Based on the DNA45230 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

PCR primers (forward and reverse) were synthesized:

forward PCR primer (45220.11) 5'-GCTGACCTGGTTCCCATCTACTCC-3' (SEQ ID NO:293)

20 TEVETSE PCR primer (45230.e1) 5'-CCCACAGACACCCCATGACACTTCC-3' (SEQ ID NO:294) Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45230 sequence which had the following nucleotide sequence

iybridization probe (45230.p1)

25 screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to for construction of the cDNA libraries was isolated from human adrenal gland tissue. isolate clones encoding the PRO1433 gene using the probe oligonucleotide and one of the PCR primers. RNA 5'-AAGAATGAATTGTACAAAGCAGGTGATCTTCGAGGAGGGCTCCTGGGGCCC-3' (SEQ ID NO:295) in order to screen several libraries for a source of a full-length clone, DNA from the libraries was

ಜ PRO1433 (designated herein as DNA71184-1634 [Figure 163, SEQ ID NO:291]; and the derived protein DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

DNA71184-1634 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 185-187 and ending at the stop codon at nucleotide positions 1349-1351 (Figure 163). The predicted The entire mucleotide sequence of DNA71184-1634 is shown in Figure 163 (SEQ ID NO:291). Clone

polypeptide precursor is 388 amino acids long (Figure 164). The full-length PRO1433 protein shown in Figure length PRO1433 sequence shown in Figure 164 (SEQ ID NO:292) evidences the presence of the following: a 164 has an estimated molecular weight of about 43,831 dalrons and a pl of about 9.64. Analysis of the full-

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amino acid 228 to about amino acid 231 and potential N-myristolation sites from about amino acid 10 to about about amino scid 60 to about amino acid 63, from about amino acid 173 to about amino acid 176 and from about 89, from about amino acid 120 to about amino acid 125, from about amino acid 169 to about amino acid 174, transmembrane domain from about amino acid 76 to about amino acid 97, potential N-glycosylntion sites from amino acid 15, from about amino ocid 41 to about amino acid 46, from about amino acid 84 to about amino acid

DNA71184-1634 has been deposited with ATCC on September 22, 1998 and is assigned ATCC deposit no. from about amino acid 229 to about amino acid 234, from about amino acid 240 to about amino acid 245, from about amino acid 318 to about amino acid 323 and from about amino acid 378 to about amino acid 383. Clone 203266.

5 alignment analysis of the full-length sequence shown in Figure 164 (SEQ ID NO:292), evidenced significant CEF59A1_4, S67138, MTV050_3, S75135 and S12411. omology between the PRO1433 amino acid sequence and the following Dayhoff sequences: CELW01A11_4, An analysis of the Dayboff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

EXAMPLE 86: Isolation of cDNA clones Encoding Human PRO1490.

20 15 in Example 1 above. This consensus sequence is herein designated DNA67006. Based on the DNA67006 the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

PCR primers (forward and reverse) were synthesized

sequence which had the following nucleotide sequence Additionally, a symbetic oligonucleotide hybridization probe was constructed from the consensus DNA 57006 EXYERS PCR primer (67006.11). 5'-GCCACCTCCATGCTAACGCGG-3' (SEQ ID NO:299) forward PCR primer (67006.11) 5'-CTTCCTCTGTGGGTGGACCATGTG-3' (SEQ ID NO:298)

25 hybridization probe (67006,p1)

5'-CCAAGGTCCTCGCTAAGAAGGAGCTGCTCTACGTGCCCCTCATCO-3' (SEQ ID NO:300)

isolate clones encoding the PRO1490 gene using the probe oligonucleotide and one of the PCR primers. RNA screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to in order to screen several libraries for a source of a full-length clone, DNA from the libraries was

ಆ for construction of the cDNA libraries was isolated from human adrenal gland tissue. DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

PRO1490 (designated herein as DNA71213-1659 [Figure 165, SEQ ID NO:296]; and the derived protein sequence for PRO1490.

ઝ DNA 71213-1659 contains a single open reading frame with an apparent translational initiation site at aucleotide polypeptide precursor is 368 amino acids long (Figure 166). The full-length PRO1490 protein shown in Figure positioms 272-274 and ending at the stop codon at nucleotide positions 1376-1378 (Figure 165). The predicted The entire nucleotide sequence of DNA71213-1659 is shown in Figure 165 (SEQ ID NO:296). Cloud

166 has an estimated molecular weight of about 42,550 daltons and a pf of about 9.11. Analysis of the full-length PRO1490 sequence shown in Figure 166 (SEQ ID NO:297) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, transmembrane domains from about amino acid 317 on about amino acid 323 and from about amino acid 335 to about amino acid 352 and tyrosine kinase phosphorylation sites from about amino acid 160 to about amino acid 168 and from about amino acid 161 to about amino acid 168. Clone DNA71213-1659 has been deposited with ATCC on October 27, 1998 and is assigned ATCC deposit no. 20340).

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLASTZ sequence alignment malysis of the full-length sequence shown in Figure 166 (SEQ ID NO:297), evidenced significant homology between the PRO1490 amino acid sequence and the following Dayhoff sequences: ASZ144_1, S60478, P_R99249, P_R89712, YBP2_YEAST, S54641, CELTD5H4_15, CELF28B3_1, CELZK40_1 and YULUS ECOLUM

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EXAMPLE 82: Isolation of cDNA clones Encoding Human PRO1482.

A cDNA clone (DNA71234-1651) encoting a native human PRO1482 polypeptide was identified by 15 a yeast screen, in a human adrenal gland cDNA library that preferentially represents the 5' ends of the primary cDNA clones.

The full-length DNA71234-1651 clone shown in Figure 167 commins a single open (rading frame with an apparent translational initiation site at nucleotide positions 33-35 and ending at the stop codon at nucleotide positions 462-464 (Figure 167). The predicted polypeptide precursor is 143 amino acids long (Figure 168). The full-length PRO1482 protein shown in Figure 168 has an estimated molecular weight of about 15,624 daltons and a p1 of about 9.58. Analysis of the full-length PRO1482 sequence shown in Figure 168 (SEQ ID NO:302) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28. Clone DNA71234-1651 has been deposited with ATCC on October 27, 1998 and is assigned ATCC deposit no.

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An analysis of the Dayhoff dalabase (version 35.48 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-tength sequence shown in Figure 168 (SEQ ID NO:302), evidenced significant bomology between the PRO1482 amino acid sequence and the following Dayhoff sequences: A18267_3.

EXAMPLE 88: Isolation of cDNA clones Encoding Human PRO1446

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmacetaticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a pancreatic idet cell library. The homology search was performed using the computer program BLAST or BLAST2 (Altshal et al., Methods in Enzymology, 266:460-480 (1996)). Those computers program BLAST score of 70 (or in some cases 90) or greater that did not encode known provides were clustered and assembled into a consensus DNA sequence with the program "plurap" (Phil Green,

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University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56514.

In light of the sequence homology between the DNA56514 sequence and an EST sequence contained within the Incyre EST 2380344, the clone including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 169 and is herein designated as DNA71277-1636.

The full length clone shown in Figure 169 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 152-154 and ending at the stop codon found at modeotide positions 479-481 (Figure 169; SEQ ID NO:303). The predicated polypeptide precursor (Figure 170, SEQ ID NO:304) is 109 amino acids long with a signal peptide at about amino acids 1-15 of SEQ ID NO:304. PRO1446 has a calculated molecular weight of approximately 11,822 daltons and an estimated pl of approximately 8,63. Clone DNA71277-1636 was deposited with the ATCC on September 22, 1998 and it assigned ATCC deposit

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An analysis of the Dayboff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 170 (SEQ ID NO.304), revealed sequence identity 15 between the PRO1446 amino acid sequence and the following Dayboff sequences (data incorporated herein):
P33_CANFA, P53_FELCA, LRP1_HSV1F, OSU57338_1, S75842, P_P93722, AF002189_1, B70408, S54309
and S53365. The first in this list is further described in Kraegel, et al., Cancer Lett., 92(2):181-186 (1995)

EXAMPLE 89: Isolation of cDNA clones Encoding Human PRO1558

- Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated Incyte EST cluster sequence no. 86390. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA databases (LIPESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST.
- 25 or BLAST2 (Altehul et al., <u>Methods in Enzymology, 266</u>:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA58842.
- In light of the sequence homology between the DNA58842 sequence and an EST sequence contained

 Within the Incyne EST clone no. 3746964, the Incyne EST clone no. 3746964 was purchased and the cDNA insert

 was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 171 and is herein designated

 as DNA71282-1668.

Clone DNA/17282-1668 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 84-86 and ending at the stop codon at nucleotide positions 870-872 (Figure 171). The 53 predicted polypepitde procursor is 262 amino acids long (Figure 172). The full-length PRO1558 protein shown in Figure 172 has an estimated molecular weight of about 28,899 dattons and a p1 of about 8.80. Analysis of the full-length PRO1558 acquence shown in Figure 172 (SEQ ID NO:306) evidences the presence of the

arnino acid 115, from about amino acid 205 to about amino avid 210 and from about amino acid 255 to about assigned ATCC deposit no. 203312. 39 to about aminn acid 42. Clone DNA71282-1668 has been deposited with ATCC on October 6, 1998 and is amino acid 260 and amidation sites from about amino acid 31 to about amino acid 34 and from about amino acid to about amino acid 27, from about amino acid 28 to about amino acid 33, from about amino acid 110 to about glycosylation site from about amino acid 190 to about amino acid 193, a tyrosine kinase phosphorylation site from about amino acid 238 to about amino acid 246, potential N-myristolation sites from about amino acid 22 amino acid 8 to about amino acid 30 and from about amino acid 109 to about amino acid 130, a potential N following: a signal peptide from about amino acid I to about amino acid 25, transmembrane domains from about

5 alignment analysis of the full-length sequence shown in Figure 172 (SEQ ID NO:306), evidenced significant MXU24657_3, CAMT_EUCGU, MSU20736_1, P_R29515, B70431, JC4004, CEY32B12A_3, CELF53B3_7 homology between the PRO1558 amino acid sequence and the following Daythoff sequences: AF075724_2, An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

2 EXAMPLE 90: Isolation of cDNA clones Encoding Human PRO1604

BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 256:460-480 (1996)]. Those comparisons Washington, Scartle, Washington). This consensus sequence is designated herein "DNA67237", resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were database, to identify homologous EST sequences. The search was performed using the computer program clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of then compared to various EST databases including public EST databases (e.g. GenBank), and the LIFESEQ was searched. Incyte EST No. 3550440 was identified as having homology to HDGF. EST No. 3550440 was An expressed sequence tag (EST) DNA database (LIFESEQ*, Incyte Pharmaceuticals, Palo Alto, CA)

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25 LIFESEQ® database, the clone containing Incyte EST No. 3367060 was purchased and the cDNA insert was ID NO:307). obtained and sequenced to obtain the entire coding sequence of PRO1604 which is shown in Figure 173 (SEQ In light of the sequence homology between the DNA67237 sequence and EST no. 3367060 from the

မ polypepide presursor is 671 amino acids long. The full-length PRO1604 protein shown in Figure 174 has an 51, 365-370, and 367-372; and a cell attachment sequence at about amino acids 661-663. peptide at about armino acids 1-13; potential cAMP- and cGMP-dependent protein kinase phosphorylation sites estimated molecular weight of about 74,317 daltons and a pl of about 7.62. Additional features include a signal at about amino acids 156-159, 171-174, and 451-454; potential N-myristoyiation sites at about amino acids 46site at inveleocide positions 65-67 and an apparent stop codon at nucleotide positions 2078-2080. The predicted Clone DNA71286-1687 contains a single open reading frame with an apparent translational initiation

ä alignment analysis of the full-length sequence shown in Figure 174 (SEQ ID NO:308), revealed significant bomology between the PRO1604 amino acid sequence and Dayhoff sequence no. P_W37483. Homology was An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

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also shown between the PRO1604 amino acid sequence and the following additional Dayhoff sequences AF063020_1, P_R66727, P_W37482, JC5661, CEC25A1_11, CEU33058_1, I38073, MST2_DROHY, and

Clone: DNA71286-1687 was deposited with the ATCC on October 20, 1998, and is assigned ATCC

EXAMPLE 91: Isolation of cDNA clones Encoding Human PRO1491

in Example 1 above. This consensus sequence is herein designated DNA67202. Bused on the DNA67202 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

<u></u> the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for

PCR primers (forward and reverse) were synthesized.

forward PCR primer (67202.11) 5'-CAACGCAGCCGTGATAAACAAGTGG-3' (SEQ ID NO:311) everse PCR primer (67202.rl) 5'-GCTTGGACATGTACCAGGCCGTGG-3' (SEQ ID NO:312)

Additionally, a symbetic oligonucleotide hybridization probe was constructed from the consensus DNA67202

15 sequence which had the following nucleotide sequence

hybridization probe (67202.p1)

5'-GGCCAGACTGATTTGCTCAATTCCTGGAAGTGATGGGGCAGATAC-3' (SEQ ID NO:313)

20 PRO1491 (designated herein as DNA71883-1660 [Figure 175, SEQ ID NO:309]; and the derived protein DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for RNA for construction of the cDNA libraries was isolated from human aortic endothelial cell tissue.

sequence for PRO1491.

ö 25 acid 139 to about amino acid 142, from about amino acid 607 to about amino acid 610 and from about amino 32 to about arntho acid 37. Clone DNA71883-1660 has been deposited with ATCC on November 17, 1998 and acid 724 to about amino acid 727, a tytosine kinase phosphorylation site from about amino acid 571 to about positions 107-109 and ending at the stop codon at nucleotide positions 2438-2440 (Figure 175). The predicted DNA71883-1660 contains a single open reading frame with an apparent translational initiation site at nucleotide signal peptide from about amino acid 1 to about amino acid 36, potential N-glycosylation sites from about amino length PRO1491 sequence shown in Figure 176 (SEQ ID NO:310) evidences the presence of the following: a polypeptide precursor is 777 amino acids long (Figure 176). The full-length PRO1491 protein shown in Figure amino acid 576 and a gram-positive cocci surface protein anchoring hexapeptide sequence from about amino acid 176 has an estimated molecular weight of about 89,651 daltons and a pl of about 7.97. Analysis of the full The entire nucleotide sequence of DNA71883-1660 is shown in Figure 175 (SEQ ID NO:309). Closs

35 homology between the PRO1491 amino acid sequence and the following Dayhoff sequences: GGU28240_1, alignment analysis of the full-length sequence shown in Figure 176 (SEQ ID NO:310), evidenced significan An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

is assigned ATCC deposit no. 203475.

MUSC.L., D49423, MMSEMH_1, AB002329_1, AF022947_1, HSU33920_1, HUMCUCA19_1, G01856 and AF022946_1.

EXAMPLE 92: Isolation of cDNA clones Encoding Human PRO1431

An expressed sequence ug (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Pulo Alto, CA) was searched and an EST (isolated from adult brain stem titsue) was identified (1370141, DNA66505) which showed homology to SH3. RNA for construction of cDNA libraries was isolated from human hone marrow. Afull length cDNA corresponding to the isolated EST was isolated using an in vitro cloning technique (DNA73401-1633) in pRK5.

The cDNA libraries used to isolate the cDNA clones encoding human PRO1431 were constructed by 10 standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo of Containing a Notl site, linked with blant to Sall hemikinased adaptors, cleaved with Notl, sized appropriately by get electrophoresia, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRKXB is a precursor of pRKSD that does not contain the Sfil site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique Xhol and Notl.

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A cDNA clone was sequenced in entirety. The entire nucleotide requence of DNA73401-1633 (SEQ

D NO:314) is shown in Figure 177. Clone DNA73401-1633 contains a single open reading frame with an
apparent translational initiation site at about nucleotide positions 630-632 and a stop codon at about nucleotide
positions 1740-1742. The predicted polypeptide precursor encoded by DNA73401-1633 is 370 amino acids long.

Clone DNA73401 (designated as DNA73402-1633) has been deposited with ATCC and is assigned ATCC

20 deposit no. 203273.

Based sequence alignment analysis (using the ALIGN computer program) of the full-length sequence. PRO1431 shows significant amino acid sequence identity to SH17_HUMAN, an SH3 containing protein known as SH3P17. Additional significant identity score were found with D89164_1, AF032118_1, EXLP_TOBAC, YHR4_YEAST, S46992, RATP130CAS_2, AF043259_1, RATP130CAS_1 and MYSC_ACACA.

EXAMPLE 23: Isolation of cDNA clones Encoding Human PRO1563

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A consensus DNA requence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA67191. Based on the DNA67191 consensus sequence, oligonucleoiddes were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for pro1563.

30

PCR primers (forward and reverse) were synthesized:

REMERSE PCR primer (67191.41) 5'-CCCTGAAGCTGCCAGATGGCTCC-3' (SEQ ID NO:318)

35 Additionally, a synthetic oligonucleotide by bridization probe was constructed from the consensus DNA67191 sequence which had the following nucleotide sequence

hybridization probe (67191.p1)

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5'-CCACAGATGTGGTACTGCCTGGGGCAGTCAGCTTGCGCTACAG-3' (SEQ ID NO:320)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1563 gene using the probe oligonatelentide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow issue.

5 DNA requencing of the clones isolated as described above gave the full-length DNA requence for PRO1563 (designated herein as DNA73492-1671 [Figures 179A-B, SEQ ID NO:316]; and the derived protein sequence for PRO1563.

ઝ 25 8 12 5 sequence from about amino acid 358 to about amino acid 367. Clone DNA73492-1671 has been deposited with nucleotide positions 419-421 and ending at the stop codon at nucleotide positions 2930-2932 (Figures 179A-B) 684, from about amino acid 682 to about amino acid 687, and from about amino acid 763 to about amino acid acid 560, from about amino acid 577 to about amino acid 582, from about amino acid 679 to about amino acid acid 121 to about amino acid 126, from about amino acid 125 to about amino acid 130, from about amino acid about arnino acid 68 to about amino acid 71, glycosaminoglycan attachment sites from about amino acid 188 to of the full-length PRO1563 sequence shown in Figure 180 (SEQ ID NO:317) evidences the presence of the ATCC on October 6, 1998 and is assigned ATCC deposit no. 203324. about amino acid 24 to about amino acid 45 and a neutral zinc metallopeptidase, zinc-binding region signature amino acid 837, leucine zipper pattern sequences from about amino acid 17 to about amino acid 38 and from 768, amidation sites from about amino acid 560 to about amino acid 563 and from about amino acid 834 to about amino acid 357, from about amino acid 539 to about amino acid 544, from about amino acid 555 to about amino about amino acid 179, from about amino acid 323 to about amino acid 328, from about amino acid 352 to about to about amino acid 172, from about amino acid 168 to about amino acid 173, from about amino acid 174 to 130 to about amino acid 135, from about amino acid 147 to about amino acid 152, from about amino acid 167 about amino acid 5 to about amino acid 10, from about amino acid 19 to about amino acid 24, from about amino phosphorylation site from about amino acid 730 to about amino acid 736, potential N-myristolation sites from protein kinase phosphorylation site from about amino acid 182 to about amino acid 185, a tyrosius kinase about amino acid 191 and from about amino acid 772 to about amino acid 775, a cAMP- and cGMP-dependent following: a signal peptide from about amino acid 1 to about amino acid 48, a potential N-glycosylation site from shown in Figure 180 has an estimated molecular weight of about 90, 167 daltons and a pl of about 8.39. Analysis The predicted polypeptide precursor is 837 amino acids long (Figure 180). The full-length PRO1563 protein Clone DNA73492-1671 contains a single open reading frame with an apparent translational initiation site at The entire nucleotide sequence of DNA73492-1671 is shown in Figures 179A-B (SEQ ID NO:316)

An analysis of the Dayboff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 180 (SEQ ID NO.317), evidenced significant homology between the PRO1563 amino acid sequence and the following Dayhoff sequences: AB014588_1, 35 D67076_1, AB001735_1, P_W47028, AB002364_1, P_W47029, GEN13695, P_R40823, AF005665_1 and DISA_TRIGA.

EXAMPLE 94: Isolation of cDNA clones Encoding Human PRO1565

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA67183. Based on an observed homology between the DNA67183 consensus sequence and an EST sequence contained within largue EST clume no. 2510320, largue EST clone no. 2510320 was purchased and its insert was obtained and sequenced. That insert sequence is shown in Figure 181 and its herein designated DNA73727-1673 (SEQ ID NO:321).

20 ᅜ 5 Clone DNA73727-1673 has been deposited with ATCC on November 3, 1998 and is assigned ATCC deposit a microbodies C-terminal targeting signal sequence from about amino acid 315 to about amino acid 317 and a from about amino acid 215 to about amino acid 220 and from about amino acid 272 to about amino acid 277, 38, from about amino acid 95 to about amino acid 100, from about amino acid 116 to about amino acid 121, about amino acid 92 to about amino acid 95, from about amino acid 70 to about amino acid 73, from about cytochronse C family heme-binding site signature sequence from about amino acid 9 to about amino acid 14. acid 239 to about amino acid 242, potential N-myristolation sites from about amino acid 33 to about amino acid acid 148 to about amino acid 151, from about amino acid 192 to about amino acid 195 and from about amino amino acid 85 to about amino acid 88, from about amino acid 133 to about amino acid 136, from about amino amino acid 97 and from about amino acid 180 to about amino acid 183, glycosaminoglycan attachment sites from about amino acid 25 to about amino acid 47, potential N-glycosylation sites from about amino acid 94 to about length PRO1565 sequence shown in Figure 182 (SEQ ID NO:322) evidences the presence of the following: a polypeptide precursor is 317 amino acids long (Figure 182). The full-length PRO1565 protein shown in Figure DNA73727-1673 comains a single open reading frame with an apparent translational initiation site at nucleotide signal peptide from about amino acid 1 to about amino acid 40, a potential type II transmembrane domain from 182 has an estimated molecular weight of about 37,130 daltons and a pl of about 5.18. Analysis of the fullpositions 59-61 and ending at the stop codon at nucleotide positions 1010-1012 (Figure 181). The predicted The entire nucleoside sequence of DNA73727-1673 is shown in Figure 181 (SEQ ID NO:321). Clone

An analysis of the Dayhoff database (vertion 35.45 SwitsProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 182 (SEQ ID NO:322), evidenced significant homology between the PRO1565 amino acid sequence and the following Dayhoff sequences: AF051425_1, P_R65490, P_R65488, GRPE_STAAU, RNU31330_1, ACCD_BRANA, D50558_1, HUMAMYAB3_1, P_W34452 and P_P50629.

EXAMPLE 95: Isolation of cDNA clones Encoding Human PRO1571

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A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA69559. Based on homology observed between the DNA69559 consensus sequence and an EST sequence contained within the Incyte EST clone no. 3140760, Incyte EST clone no. 3140760, was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 183 and is herein designated as DNA7373D-1679.

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Clone DNA73730-1679 contains a single open reading frame with an apparent translational initiation

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site at medeotide positions 90-92 and ending at the stop codom at nucleotide positions 807-809 (Figure 183). The predicted polypeptide procursor is 239 amino acids long (Figure 184). The full-length PRO1571 protein shown in Figure 184 has an estimated molecular weight of about 25,699 daltons and a pl of about 8.99. Analysis of the full-length PRO1571 sequence shown in Figure 184 (SEQ ID NO.324) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21 and transmembrane domains from about amino acid 21 and transmembrane domains from about amino acid 82 to about amino acid 10.5 from about amino acid 115 to about amino acid 141 and from about amino acid 100 about amino acid 100 acoustics.

5 about amino acid 82 to about amino acid 103, from about amino acid 115 to about amino acid 141 and from about amino acid 160 to about amino acid 182. Clone DNA73730-1679 has been deposited with ATCC on October 6, 1998 and is assigned ATCC deposit no. 203320.
An analysis of the Dayboff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

alignment analysis of the full-length sequence shown in Figure 184 (SEQ ID NO.324), evidenced significant 10 homology between the PRO1571 amino acid sequence and the following Dayhoff sequences: AP072128 1, AB000712_1, AB000714_1, AF007189_1, AF000959_1, AF0068863_1, P_W15288, PM22_HUMAN, P_R30056 and LSU46824_1.

EXAMPLE 96: Isolation of cDNA clones Encoding Human PRQ1572

Using the method described in Example 1 above, a consensus sequence was obtained. The consensus sequence is designated herein "DNA69560". Based on the DNA69560 consensus sequence and other information provided herein, a clone including another EST (Incyte DNA2051424) from the assembly was purchased and exquenced.

The entire coding sequence of PRO1573 is included in Figure 185 (SEQ ID NO:325). Close DNA73734-1680 comains a single open reading frame with an apparent translational initiation site at medicoride positions 90-92 and an apparent stop codon at nucleotide positions 873-875. The predicted polypeptide precursor is 261 amino acids long. The signal peptide is at about amino acids 1-23 and the transmembrane domains are at about amino acids 81-100, 121-141, and 173-194 of SEQ ID NO:326. One or more of the transmembrane domains can be deleted or inactivated. The locations of a N-glycosylation site, N-myristoylation site, a syrosine domains can be deleted or inactivated. The locations of a N-glycosylation site, N-myristoylation site are indicated in Figure 186. Clone DNA73734-1680 has been deposited with the ATCC and is assigned ATCC deposit no. 203363. The full-length PRO1572 protein shown in Figure 186 has an estimated molecular weight of about 27, 856 daltons

An analysis of the Dayhoff database (version 35.45 SwissFrot 35), using a WU-BLAST2 sequence 30 alignment analysis of the full-length sequence shown in Figure 186 (SEQ ID NO:326), revealed sequence identity between the PRO1572 amino scid sequence and the following Dayhoff sequences (incorporated herein): AF072127_1, HSU89916_1, AB000713_1, AB000714_1, AB000712_1, AF000959_1, AF072128_1, AF068863_1, P_W29881, and P_w58869.

and a pl of about 8.5.

35 EXAMPLE 97: Isolation of cDNA clones Encoding Human PRO1573

EST 3628990 was identified in an incyte Database, (LIFESEQ*, Incyte Pharmaceuticals, Palo Alto, CA) and extended in a comparison to other sequences in databases to form an assembly. The alignment search

was performed using the computer program BLAST or BLAST2 (Atschul et al., Methods in hinzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seanle, Washington). The consensus sequence is designated herein "DNA 60561"

Based on the DNA69561 consensus sequence and other information provided herein, a clone including another EST (Incyre DNA3752657) from the assembly was purchased and sequenced. This clone came from a breast numor tissue library.

The entire coding sequence of PRO1573 is included in Figure 187 (SEQ ID NO:327). Clone 10 DNA73735-1681 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 97-99 and an apparent stop codon at nucleotide positions 772-774. The predicted polypeptide precursor is 225 amino acids long. The signal peptide is at about amino acids 1-17 and the transmembrane domains are at about amino acids 82-101, 118-145, and 164-188 of SEQ ID NO:328. One or more of the transmembrane domains can be deleted or inactivated. A phosphorylation site, amidation site, and N-myristoylation sites are thown in Figure 188. Clone DNA73735-1681 has been deposited with ATCC and is assigned ATCC deposit no. 203356. The full-length PRO1573 protein shown in Figure 188 has an estimated molecular weight of about 24,845 daltons and a p1 of about 9.07.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 188 (SEQ ID NO:328), revealed sequence identify 20 between the PRO1573 amino acid sequence and the following Dayhoff sequences (incorporated herein):

APO07189_1, AB000714_1, AB000713_1, AB000712_1, A39484, AF000959_1, AF072127_, AF072128_1, AF088863_1 and AF077739_1.

EXAMPLE 98: Isolation of cDNA clones Encoding Human PRO1488

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An expressed sequence tag (EST) DNA database (LIFESEQ*, Incyte Pharmaceuticals, Palo Alto, CA) was searched and EST No. 3639112H1 was ideatified as having homology to CPE-R. EST No. 3639112H1 is designated herein as "DNA69562". EST clone 3639112H1, which was derived from a lung tissue library of a 20-week old fetus who died from Patas's syndrome, was purchasted and the cDNA intert was obtained and sequenced in its emitrety. The entire nucleotide sequence of PRO1488 is shown in Figure 189 (SEQ ID NO.3259), and is designated herein as DNA73736-1657. DNA73736-1657 contains a single open reading frame with an apparent translational initiation site as mucleotide positions 6-8 and a step codon at mecleotide positions with an apparent translational initiation site at mucleotide positions 6-8 and a step codon at mecleotide positions 6-6-686 (Figure 189; SEQ ID NO.3259). The predicted polypeptide precursor is 220 antino acids long.

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The full-length PRO1488 protein shown in Figure 190 has an estimated molecular weight of about 23,292 dations and a p1 of about 8.43. Four transmembrane domains have been identified as being located at about amino acid positions 8-30, 82-102, 121-140, and 166-186.

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An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST? sequence alignment analysis of the full-length sequence shown in Figure 190 (SEQ ID NO:330), revealed significant

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homology between the PRO1488 amino acid sequence and Dayboff sequence AB000712_1. Homology was also found between the PRO1488 amino acid sequence and the following additional Dayboff sequences: AB000714_1, AF007189_1, AF000959_1, P_W63697, MMU82758_1, AF072127_1, AF072128_1, HSU89916_1, AF068863_1, CPAF000418_1, and AF077739_1.

Clone DNA73736-1657 was deposited with the ATCC on November 17, 1998, and is assigned ATCC deposit no. 203466.

EXAMPLE 99: Isolation of cDNA clones Encoding Human PRO1489.

A consensus DNA sequence was assembled relative to other EST sequences using pirmp as described in Example 1 above. This consensus sequence is herein designated DNA69563. Based upon an observed 10 sequence similarity between the DNA69563 consensus sequence and an EST sequence contained within the Incyte EST clone no. 3376608, Incyte EST clone no. 3376608, Incyte EST clone and an experience and its insert obtained and sequenced. That insert is herein designated DNA73737-1658.

The entire nucleotide sequence of DNA73737-1658 is shown in Figure 191 (SEQ ID NO.331). Clone DNA73737-1658 contains a single open reading frame with an apparent translational initiation site at nucleotide 15 positions 264-266 and ending at the stop codon at nucleotide positions 783-785 (Figure 191). The predicted polypeptide precursor is 173 amino acids long (Figure 192). The full-length PRO1489 protein shown in Figure 192 has an estimated molecular weight of about 18,938 daltons and a p1 of about 9.99. Analysis of the full-length PRO1489 sequence shown in Figure 192 (SEQ ID NO.332) evidences the presence of the following: transnermbrane domains from about amino acid 31 to about amino acid 51, from about amino acid 70 and from about amino acid 112 to about amino acid 133 and a potential N-glycosylation site from about amino acid 161 to about amino acid 164. Clone DNA73737-1658 has been deposited with ATCC on October 27, 1998 and it assigned ATCC deposit no. 203412.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLASTZ sequence alignment analysis of the full-length sequence shown in Figure 192 (SEQ ID NO:332), evidenced significant 25 homology between the PRO1489 animo acid sequence and the following Dayhoff sequences: AF007189_1, AB000712_1, AF000959_1, MMU82758_1, AF035814_1, AF072127_1, AF072128_1, HSU89916_1, AF068863_1 and PPU50051_1.

EXAMPLE 100: Isolation of cDNA clones Encoding Human PRO1474.

30 An expressed sequence tag (EST) DNA database (LIFESEQ*, Incyte Pharmaceutical, Palo Alto, CA) was searched and an EST was identified. This EST showed homology to pancreatic secretory trypsin inhibitor.

The clone which included this EST was purchased from Incyte (it came from a uterime cervical tissue library) and sequenced in full to reveal the nucleic acid of SEQ ID NO:333, which encodes PRO1474.

The entire nucleotide sequence of PRO1474 is shown in Figure 193 (SEQ ID NO:333). Clone DNA73739-1645 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 45-47 and a stop codon at nucleotide positions 300-302 (Figure 193; SEQ ID NO:333). The predicted polypoptide precursor is 85 amino acids long. As indicated in Figure 194, the Kazal serine protease thatbitor

family signature begins at about amino acid 45 of SEQ ID NO:334. Also indicated in Figure 194 is a region conserved in integrin alpha chains (beginning at about amino acid 32 of SEQ ID NO:334). Clone DNA/3739, 1645 has been deposited with the ATCC and is assigned ATCC deposit no. 203270. The full-length PRO1474 protein shown in Figure 194 has an estimated molecular weight of about 9,232 dultons and a pt of about 7,94.

An analysis of the Dayhoff database (version 35.45 SwitsProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 194 (SEQ ID NO:334), revealed sequence identity between the PRO1474 amino acid sequence and the following Dayhoff sequences (all ovonmucoids, data incorporated herein by reference): IOVO_FRAER, IOVO_FRAAF, IOVO_FRACO, IOVO_CYRMO, IOVO_STRCA, H61492, C61589, IOVO_POLPI, D61589, and IOVO_TURME.

10 EXAMPLE 101: Isolation of cDNA clones Encoding Human PRO1508

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte Cluster No. 34523, also referred herein as "DNA10047". This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public and private EST databases (e.g., GenBank and (LIFESEQ®) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymethogy, 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seatule, Washington). The consensus sequence obtained therefrom is herein designated "DNA557723".

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20 In light of the sequence homology between the DNA55723 sequence a sequence contained within Incyte EST no. 2989064, the EST clone 2989064 was purchased and the cDNA insert was obtained and sequenced in its entirety. The sequence of this cDNA insert is shown in Figure 195 and is herein designated as *DNA73742-1662*.

The full length clone shown in Figure 195 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 70 to 72 and ending at the stop codon found at nucleotide positions 514 to 516 (Figure 195; SEQ ID NO:335). The predicted polypeptide precursor (Figure 196, SEQ ID NO:335) is 148 amino acids long. Other features of the PRO1508 protein include: a signal sequence at about amino acids 1-30; a tyrosine kinase phosphorylation motif at about amino acids 27-32, 28-33, and 140-145. PRO1508 has a calculated molecular weight of approximately 17, 183 dultons and an estimated pt of approximately 8.77. Cloue DNA73742-1662 was deposited with the ATCC on October 6, 1998 and is assigned ATCC deposit no. 203316.

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An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLASTZ sequence alignment analysis of the full-length sequence shown in Figure 196 (SEQ ID NO:336), revealed some homology between the PRO1508 amino acid sequence and the following Dayhoff sequences: HSAJ3728_1; P_R74962; P_R74941; AF053074_1; F69515; S20706; RPBL_PLAFD; A20587_1; A51861_1; and 575947.

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EXAMPLE 102: Isolation of cDNA clones Encoding Human PRO1555

Use of the signal sequence algorithm desteribed in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST cluster no. 521, and also referred to herein as "DNA10316". This EST cluster sequence was then compared to a variety of expressed sequence ug (EST) databases which included public EST databases (e.g., GenBank) and the LIFESEQ® database to identify sexisting bomologies. The homology search was performed using the computer program BLAST or BLAST? (Albahil et al., Methods in Enzymology 256:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a contensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated "DNA56374".

In light of the sequence homology between the DNA56374 sequence and an EST sequence contained within Incyte EST no. 2855769, EST no. 2855769 was purchased and the cDNA insert was obtained and sequenced. EST no. 2855769 was derived from a library constructed from female breast fat tissue. The sequence of this cDNA insert is shown in Figure 197 and is herein designated as DNA73744-1665.

The full length clone shown in Figure 197 contained a single open reading frame with an apparent 15 translational initiation site at nucleotide positions 90 to 92 and ending at the stop codon found at nucleotide positions 828 to 820 (Figure 197; SEQ ID NO:337). The predicted polypeptide precursor (Figure 198, SEQ ID NO:338) is 246 amino acids long. PRO1555 has a calculated molecular weight of approximately 26,261 daltous and an estimated pl of approximately 5.65. Additional features include: a signal peptide at about amino acids 1-31; transprembrane domains at about amino acids 11-31 and 195-217; a potential N-glycosylation site

20 at about amino acids 111-114; potential case in kinase II phosphorylation sites at about amino acids 2-5, 98-101, and 191-194; and potential N-myristoylation sites at about amino acids 146-151, and 192-197.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 requence allignment analysis of the full-length sequence shown in Figure 198 (SEQ ID NO:338), revealed some homology between the PRO1555 amino acid sequence and the following Dayhoff sequences: YKA4_CAEEL, 25 AB014541_1, HVSX99518_2, SSU63019_1, GEN14286, MMU68267_1, XP2_XENLA, ICP4_HSV11, P_W40200, and AE001360_1.

Close DNA73744-1665 was deposited with the ATCC on October 6, 1998, and is assigned ATCC deposit no. 203322.

30 EXAMPLE 103: Isolation of cDNA clones Encoding Human PRO1485

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein "DNA4791". Based on the DNA4791 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1485.

PCR primers (2 forward and 2 reverse) were symbosized:

forward PCR primer_L; 5'CCCTCCAAGGATGACAAAGGCGC 3' (SEQ ID NO:341);

Interest PCR primer 2: 5"GTCAGCAGCTTTCTTGCCCTAAATCAGG 3" (SEQ ID NO:342);
**EXPLISE PCR primer 1: 5"ATCTCAGGCGGCATCCTGTCAGCC 3" (SEQ ID NO:343); and
**EXPLISE PCR primer 2: 5"GTGGATGCCTGCAAGAAGGTTGGG 3" (SEQ ID NO:344).

Additionally, a synthetic oligonucleoxide hybridization probe was constructed from the consensus DNA44791 sequence which had the following nucleoxide sequence:

hybridization probe 5'AGCTTTCTTGCCCTAAATCAGGCCAGCCTCATCAGTCGCTGTGAC 3' (SEQ ID NO:345)

In order to serren several libraries for a source of a full-length clone. DNA from the libraries was serrened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1485 gene using the probe oligomucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human testis.

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DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1485 (destignated herein as DNA73744-1654 [Figure 199, SEQ ID NO:339]; and the derived protein sequence for PRO1485.

The entire coding sequence of PRO1485 is shown in Figure 199 (SEQ ID NO:339). Clone DNA/374615 1654 contains a single open reading frame with an apparent translational initiation site at nucleotide positions
151-153 and an apparent stop codon at nucleotide positions 595-597 of SEQ ID NO:339. The predicted
polypeptide precursor is 148 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID
NO:340. The lysozyme C signature, CAAX box, and an N-groosylation site are shown in Figure 200. Clone
DNA/3746-1654 has been deposited with ATCC and is assigned ATCC deposit no. 203411. The full-length
20 PRO1485 protein shown in Figure 200 has an estimated molecular weight of about 16,896 dalions and a p1 of
shown 6 Of

An analysis of the Dayhoff database (version 33,45 SwissProt 35), using a WU-BLAST? sequence alignment analysis of the full-length sequence shown in Figure 200 (SEQ ID NO:340), revealed sequence identity between the PRO1485 amino acid sequence and the following Dayhoff sequences: LYC_PHACO, P_R76684, 2HFL_Y, JC2144, JC5544, JC5555, JC5369, LYC2_PIG, P_R12113, and JC5380.

EXAMPLE 104: Isolation of cDNA clones Encoding Human PRO1564

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A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA67213. Based on the DNA67213 30 consensus sequence, oligonucleotides were symbosized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a close of the full-length coding sequence for

PCR primers (forward and reverse) were symbosized:

5'-GGAGAGGTGGTCGCCATGGACAG-3' (SEQ ID NO:348)

35 reverse PCR primer (67213.rl) 5'-CTGTCACTGCAAGGAGCCAACACC-3' (SEQ ID NO:349)

Additionally, a symbetic oligonucleotide by bridization probe was constructed from the consensus DNA67213 sequence which had the following nucleotide sequence

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hybridization probe (67213.p1)

S'-TATGTCGCTGCGAGGTGGTGAAAACCTCGAACTGTCTTTCAAGGC-3' (SEQ ID NO:350)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1564 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast carefnoms tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1564 (designated herein as DNA73760-1672 [Figure 201, SEQ ID NO:346]; and the derived protein sequence for PRO1564.

The entire nucleotide sequence of DNA73760-1672 is shown in Figure 201 (SEQ ID NO:346). Close 10 DNA73760-1672 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 462-464 and ending at the stop codon at nucleotide positions 2379-2381 (Figure 201). The predicted polypeptide precursor is 639 amino acids long (Figure 202). The full-length PRO1564 protein shown in Figure 202 has an estimated molecular weight of about 73,063 dations and a pl of about 6.84. Analysis of the full-length PRO1564 sequence shown in Figure 202 (SEQ ID NO:347) evidences the presence of the following: a size of arms the form about maries cold to the sequence.

15 signal peptide from about amino acid 1 to about amino acid 28, a trasnmembrane domain from about amino acid 110 to about amino acid 36, potential N-glycosylation sites from about amino acid 107 to about amino acid 110 and from about amino acid 574 to about amino acid 577, a tyrosine kinase phosphoxylation site from about amino acid 576 to about amino acid 577, potential N-myristolation sites from about amino acid 158 to about amino acid 267, potential N-myristolation sites from about amino acid 262 to about amino acid 266 to about amino acid 267, from about amino acid 267.

163, from about amino acid 236 to about amino acid 241, from about amino acid 262 to about amino acid 279 to about amino acid 279 to about amino acid 278, from about amino acid 380 to about amino acid 383 and from about amino acid 513 to about amino acid 518, an amidation site from about amino acid 110 to about amino acid 110 to about amino acid 113 and a prokaryotic membrane lipoprotein lipid arachment site from about amino acid 15 to about amino acid 25. Clone DNA73760-1672 has been deposited with ATCC on October 6, 1998 and is assigned ATCC deposit no.2033[4.

An analysis of the Dayhoff database (version 33.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 202 (SEQ ID NO:347), evidenced significant bomology between the PRO1564 amino acid sequence and the following Dayhoff sequences: MMU73819_1, HSY08564_1, P.W34470, P_R66402, PAGT_HUMAN, CEGLYSB_1, CEGLY6A_1, CEGLY6B_1, AP000006_308 and E69322.

EXAMPLE 105: Isolation of cDNA clones Encoding Human PRO1755

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Use of the signal sequence algorithm described in Example 3 above allowed Identification of an EST cluster sequence from the LIFESEQ® database, designated EST Cluster No. 141872. This EST cluster sequence was then compared to a variety of ESTs from the databases listed above to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altabul et al., Mcthods in Enzymology 266:460-480 (1996)). Those computerious resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with

the program "phrap" (Phil Green, University of Washington, Scattle, Washington). The consensus sequence obtained therefrom is herein dealgrated. "DNAS5731".

In light of the sequence homology between the DNA55731 sequence and a sequence contained within Incyte EST no. 257323, the EST clone was purchased and the cDNA insert was obtained and sequenced. Incyte clone 257323 was derived from a library constructed using RNA isolated from the hNT2 cell line (Stratagene library no. STR9372310), which was derived from a human teratocarcinoma that exhibited properties characteristic of a committed neuronal precursor at an early stage of development. The sequence of this cDNA insert is shown in Figure 203 and is herein designated "DNA76396-1698". Alternatively, the DNA76396-1698 sequence can be obtained by preparing oligonuclootide probes and primers and isolating the sequence from an appropriate library (e.g. STR9372310).

The full length clone shown in Figure 203 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 58 to 60 and ending at the stop codon found at nucleotide positions 886 to 888 (Figure 203; SEQ ID NO:351). The predicted polypeptide precursor (Figure 204, SEQ ID NO:352) is 276 amino acids long. PRO1755 has a calculated molecular weight of approximately 29,426 dahtons and an estimated p1 of approximately 9,40. Additional features include: a signal peptide sequence at about amino acids 1.31; a transmembrane domain at about unition acids 178-198; a cAMP and cGMP-dependent protein kinase phosphorylation site at about amino acids 210-213; potential N-myritroylation sites at about amino acids 117-122, 154-149, and 214-219; and a cell attachment sequence at about amino acids 149-151.

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An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 204 (SBQ ID NO:352), revealed some homology 20 between the PRO1755 anino acid sequence and the following Dayhoff sequences: APG-BRANA, P_R37743, NAU88587_1, YHL1_EBV, P_W31855, CET10B10_4, AF039404_1, PRP1_HUMAN, AF038575_1, and AR03901_1.

Clone DNA76396-1698 was deposited with the ATCC on November 17, 1998, and is assigned ATCC deposit no. 203471.

EXAMPLE 106: Isolation of cDNA clones Encoding Human PRO1757

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Use of the signal sequence algorithm described in Example 3 above allowed identification of three EST sequences from the incyte database, designated incyte EST clones no. 2007947, 2014962 and 1912034. These EST sequences were then clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Sentle, Washington). The consensus sequence obtained therefrom is berein designated as DNA56054.

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In light of the sequence homology between the DNA56054 sequence and a sequence comtained within the Incyc EST clone no. 2007947, the Incyc EST clone no. 2007947 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 205 and is terriin designated as DNA76398-1699.

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Clone DNA76398-1699 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 59-61 and ending at the stop codon at nucleotide positions 422-424 (Figure 205). The

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predicated polypeptide precursor is 121 amino acids long (Figure 206). The full-length PRO1757 protein shown in Figure 206 has an estimated molecular weight of about 12,073 daltons and a pl of about 4.11. Analysis of the full-length PRO1757 sequence shown in Figure 206 (SEQ ID NO:354) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transrembrane domain from about amino acid 91 to about amino acid 40 a byte and to about amino acid 91 to about amino acid 410, a glycosaminoglycan attendment site from about amino acid 410 a bout amino acid 47, a taMP- and cGMP-dependent provein Kinase phosphorylation site from about amino acid 116 to about amino acid 119 and a potential N-myristolation site from about amino acid 91 to about amino acid 96. Clone DNA76398-1699 has been deposited with ATCC on November 17, 1998 and it assigned ATCC deposit no. 203474.

An analysis of the Dayhoff database (version 33.45 SwissProt 35), using a WU-BLAST2 sequence 10 alignment analysis of the full-length sequence shown in Figure 206 (SEQ ID NO:354), evidenced significant homology between the PRO1757 amino acid sequence and the following Dayhoff sequences: JQ0964, COLL_HSV57, HSU70136_1, AF003473_1, D89728_1, MTF1_MOUSE, AF029777_1, HSU88133_1 and P_W05321.

15 EXAMPLE 107: Isolation of cDNA clones Encoding Human PRO1758

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST cluster No. 20926. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) from the databases mentioned above, to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2.

20 (Altshul et al., Methods in Enzymology, 265:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is berein designated DNA56250.

In light of the sequence homology between the DNA56260 sequence and a sequence contained within 25 EST no. 2936330 from the LIFESEQ® database, the EST clone, which originated from a library constructed from thymus tissue of a fetus that died from anencephalus, was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 207 and is herein designated as DNA76399-1700.

The full length clone shown in Figure 207 contained a single open reading frame with an apparent 30 translational initiation site at nucleotide positions 78 to 80 and ending at the stop codon found at nucleotide positions 549-551 (Figure 207; SEQ ID NO.355). The predicted polypeptide precursor (Figure 208, SEQ ID NO.355) is 157 amino acids long. PRO1728 has a calculated molecular weight of approximately 17,681 dattons and an estimated pt of approximately 7,65. Additional features include: a signal peptide from about amino acids 1-15; a potential N-glycoxylation site at about amino acids 24-27; a cAMP- and cGMP-dependent protein kinase

35 phosphorylation site at about amino acida 27-30; a casein kinase II phosphorylation site at about amino acida 60-63; potential N-myristoylation sites at about amino acida 17-22, 50-55, 129-134, and 133-138; a cell attachment exquence at about amino acida 133-135; and a cytochrome e family hence-binding site alguature at about amino

acids 18-23.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 208 (SEQ ID NO-356), revealed significant bomology between the PRO1758 amino acid sequence and Dayhoff sequence no AC005328_2. Homology was also found between the PRO1758 amino acid sequence and Dayhoff sequence no. CELC46F2_1.

Clone DNA76399-1700 was deposited with the ATCC on November 17, 1998 and is assigned ATCC deposit no. 203472.

EXAMPLE 108: Isolation of cDNA clones Encoding Human PRO1575

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

10 in Example 1 above. This consensus sequence is designated herein as "DNA35699". Based on the DNA35699

consensus sequence, oligonucleotides were symbosized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1575.

PCR primers (forward and reverse) were synthesized:

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 forward_PCR_primers:
 CCAGCAGTGCCCCATACTCCCATAGC (35699.fl; SEQ ID No:359);

 TGACGAGTGGGATACACTGC (35699.fl; SEQ ID NO:350)

TEVERSE PCR primer: GCTCTACGGAAACTTCTGCTGTGG (35699.r1; SEQ ID NO:361)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35699 sequence which had the following nucleotide sequence:

hybidization_probe: ATTCCCAGGCGTGTCATTTGGGGATCAGCACTGATTCTGAGGTTCTGACAC (3569-p1; SEQ ID NO:362)

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In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1575 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human pancreatic tissue.

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DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1575 (designated herein as DNA76401-1683 [Figure 209, SEQ ID NO:357]; and the derived protein sequence for PRO1575.

The entire coding sequence of PRO1575 is shown in Figure 209 (SEQ ID NO;357). Clone DNA7640130 1680 contains a single open reading frame with an apparent translational initiation site at nucleotide positions
22-24 and an apparent stop codon at nucleotide positions 841-843. The predicted polypeptide precursor is 273
amito acids long. The full-length PRO1575 protein shown in Figure 210 has an estimated molecular weight of
about 30,480 datous and a pl of about 4.60. Additional features include: a signal peptide at about amino acids
1-20; a transmembrane domain at about amino acids 143-162; a potential N-glycosylation site at about amino
35 acids 100-103; and potential N-myristroylation sites at about amino acids 84-89, 103-108, 154-159, and 201-206.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 210 (SEQ ID NO:358), rewealed significant

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homology between the PRO1575 amino acid sequence and Dayhoff sequence A12005_1. Homology was also revealed between the PRO1575 amino acid sequence and the following additional Dayhoff sequences: P_P80615; P_R25297; P_R51696; A47300; PDI_DROMG; P_R49829; P_R63807; DMALPADAP_1; and DRZNF6_1.

Clone DNA76401-1683 was deposited with the ATCC on Octuber 20,1998, and is assigned ATCC

EXAMPLE 109: Isolation of cDNA clones Encoding Human PRO1787

deposit no. 203360

A consensus DNA sequence was assembled relative to other EST sequences using planp to form an assembly as described in Example 1 above. This contensus sequence is designated herein "DNA45123". Based on homology of DNA45123 to Incyte EST 3618549 identified in the assembly, as well as other discoveries and 10 information provided herein, the clone including this EST was purchased and sequenced. DNA sequencing of the clone gave the full-length DNA sequence for PRO1787 and the derived protein sequence for PRO1787.

The emire coding sequence of PRO1787 is included in Figure 211 (SEQ ID NO:363). Clone DNA76510-2504 contains a single open reading frame with an apparent translational initiation site at mackotide positions 163-165 and an apparent stop codon at nucleotide positions 970-972 of SEQ ID NO:363. The approximate locations of the signal peptide, transmembrane domain, N-glycosylationsites, N-myristoylationsites and a kinase phosphorylation site are indicated in Figure 212. The predicted polypeptide precursor is 269 amino acids long. Close DNA76510-2504 has been deposited with the ATCC and it assigned ATCC deposit no. 209477. The full-length PRO1787 protein shown in Figure 212 has an estimated molecular weight of about 20.0.2004 dattons and a p1 of about 9.02.

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An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 212 (SEQ ID NO.364), revealed sequence identity between the PRO1787 amino acid sequence and the following Dayhoff sequences: MYPO_RAT, MYPO_HUMAN, MYPO_BOVIN, GEN12838, HSSCNZB2_1, AF007783_1, HSU90716_1, P_W42015, XLU43330_1 and AF060231_1.

EXAMPLE 110: Isolation of cDNA clones Encoding Human PRO1781

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Initial DNA sequences referred to herein as DNA58070 and DNA56340 were identified using a yeast screen, in a human SK-Lu-I adenocarcinoma cell line cDNA library that preferentially represents the 5' ends of the primary cDNA clones. These sequences were clustered and assembled into a consensus DNA sequence using the computer program 'phrap'' (Phil Green, University of Washington, Seattle, Washington). The consensus sequence is designated herein as "DNA59575".

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an apparent translational initiation site at nucleotide positions 21 to 23 and ending at the stop codon found at nucleotide positions 1141-1143 (Figure 213; SEQ ID NO:365). The predicted polypeptide precursor (Figure 214, SEQ ID NO:366) is 373 amino acids long. PRO1781 has a calculated molecular weight of approximately 41,221 daltons and an estimated p1 of approximately 8.54. Additional features include: a possible signal peptide at about amino acids 1-19; a transmembrane domain at about amino acids 39-60; a tyrosine phosphorylation site at about amino acids 228-236; potential N-myritroylation sites at about amino acids 16-21, 17-22, 43-48, 45-50, 47-52, 49-54, 53-58, 58-63, 59-64, 62-67, 126-131, and 142-147; amidation sites at about amino acids 12-22. and 280-283; and a probaryotic membrane lipoprovein lipid attachment site at about amino acids 12-22.

An amalysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 214 (SEQ ID NO:366), revealed some homology 10 between the PRO1781 animo axid sequence: and the following Dayhoff sequences: CEY4510D_5, AP000001_146, P_R10576, DAC_STRSQ, CEC40H5_5, P_R35204, KPU38495_1, KPN16781_1, AP010403_1, and AP056116_14.

Clone DNA76522-2500 was deposited with the ATCC on November 17, 1998, and is assigned ATCC eposit no. 203469.

EXAMPLE 111: Isolation of cDNA clones Encoding Human PRO1556

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Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated EST Chuter No. 103158, and also referred to herein as "DNA 10398". This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and the LIFESEQ® database, to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Alakhul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seartle, Washington). The consensus sequence which therefore is herein designated DNA56417.

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In light of the sequence homology between the DNA56417 sequence and a sequence comained within Incyte EST no. 959332, EST no. 959332 was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 215 and is herein designated as DNA76579-1666.

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The full length clone shown in Figure 215 contained a single open reading frame with an apparent 30 translational initiation site at nucleotide positions 85 to 87 and ending at the stop codon found at nucleotide positions 892 to 894 (Figure 215; SEQ ID NO:371). The predicted polypeptide precursor (Figure 216, SEQ ID NO:372) is 269 amino acids long. PRO1556 has a calculated molecular weight of approximately 28,004 daltons and an estimated p1 of approximately 5.80. Additional features include: a signal peptide sequence at about amino acids 1:24; transmembrate domains at about amino acids 11:25 and 226-243; a potential N-35 glycosylation site at about amino acids 182-185, potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and potential N-myristoylation sites at about amino acids 70-73; and 70-745, 746-745, 747-7452, 749-7454, 740-7455, 747-7457, 749-7454, 740-7457, 740-7457, 740-7457, 740-7457, 740-7457, 740-7457, 740-7457, 740-7457, 740-7457, 740-7457, 740-7457, 740-7457, 740-7457, 7

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252-257, 253-258, 254-259, 255-260, 256-261, 257-262, and 259-264,

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 216 (SEQ ID NO:372), revealed some homology between the PRO1556 amimo acid sequence and the following Dayhoff sequences: T8F5_4, R23B_MOUSE, CANS_HUMAN, P_W41640, DSUS1091_1, TF2B_CHICK, DVU20660_1, S43296, P_R23962, and BRN1_HUMAN.

Clone DNA76529-1666 was deposited with the ATCC on October 6, 1998, and is assigned ATCC deposit no. 203315.

EXAMPLE 112: Isolation of cDNA clones Encoding Human PRO1759

- 10 Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST charter sequence from the Incyte database, designated DNA10571. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ*, Incyte Pharmaceuricals, Palo Alto, CA) to identify existing homologies. Once or more of the ESTs was derived from pooded cosinophils of allergic asthmatic than the compared of the
- 15 patients. The homology search was performed using the computer program BLAST or BLAST2 (Altahul et al., Methods in Enzymology, 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green. University of Washington, Scattle, Washington). The consensus sequence obtained therefrom is berein designated DNA57313.
- 20 In light of the sequence homology between the DNA57313 sequence and the Incyte EST 2434255, the close including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 217 and is herein designated as DNA76531-1701.

The full length clone shown in Figure 217 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 125-127 and ending at the stop codon found at matheotide positions 1475-1477 (Figure 217; SEQ ID NO:373). The approximate locations of the signal peptide and transmembrane domains are indicated in Figure 218, whereas the approximate locations for N-myristoyhalion sites, a lipid attachment site, an amidation site and a kinase phosphorylation site are indicated in Figure 218, sites, a lipid attachment site, an amidation site and a kinase phosphorylation site are indicated in Figure 218.

The predicted polypeptide precursor (Figure 218, SEQ ID NO:374) is 450 amino acids long. PRO1759 has a calculated molecular weight of approximately 49,765 dattons and an estimated p1 of approximately 8.14. Clone 30 DNA76531-1701 was deposited with the ATCC on November 17, 1998 and is assistanced ATCC deposit no.

0 DNA76531-1701 was deposited with the ATCC on November 17, 1998 and is assigned ATCC deposit so 203465.
An analysis of the Dayboff dambase (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

alignment analysis of the full-length sequence shown in Figure 218 (SEQID NO.374), revealed sequence identity between the PRO1759 amino acid sequence and the following Dayhoff sequences: OPDE_PSEAE 35 THII_TRYBB, S07684, RGT2_YEAST, S68362, ATSUGTRPR_1, P_W17836 (Patent application WO9715668-A2), F69587, A48076, and A45611.

EXAMPLE 113: Isolation of cDNA clones Encoding Human PRO1760.

or more of the ESTs was derived from a prostate tumor library. The homology search was performed using the proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known computer program BLAST or BLAST2 (Altshul et al., Methods in Erzymology, 266:460-480 (1996)). Those EST DNA database (LIFESEQ*, Incyte Pharmaceuticals, Palo Aito, CA) to identify existing homologies. One expressed sequence ing (EST) databases which included public EST databases (e.g., GenBank) and a proprietary Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST

cDNA insert is shown in Figure 219 and is herein designated as DNA76532-1702. including this EST was purchased and the cDNA insert was obtained and sequenced. The sequence of this In light of the sequence homology between DNA58798 sequence and the Incyte EST 3358745, the clone 5

translational initiation site at nucleotide positions 60-62 and ending at the stop codon found at nucleotide positions is 188 amino acids long. Motifs are further indicated in Figure 220. PRO1760 has a calculated molecular 624-626 (Figure 219; SEQ ID NO:375). The predicted polypeptide procursor (Figure 220, SEQ ID NO:376) deposited with the ATCC on November 17, 1998 and is assigned ATCC deposit no. 203473. weight of approximately 21,042 daltons and an estimated pl of approximately 5.36. Clone DNA76532-1702 was The full length clone shown in Figure 219 contained a single open reading frame with an apparent

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20 ATFIC12_3, APE3_YEAST, P_W22471, SAU56908_1, SCPA_STRPY, ATAC00423817, SAPURCLUS_2 between the PRO1760 amino acid sequence and the following Dayhoff sequences: CELTO7F12_2, T22118_16 alignment analysis of the full-length sequence shown in Figure 220 (SEQ ID NO:376), revealed sequence identity An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

EXAMPLE 114: Isolation of cDNA clones Encoding Human PRO1561

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DNA40630 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that for PRO1561. contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence as described in Example 1 above. This consensus sequence is herein designated DNA40630. Based on the cycles of BLAST and phrap to extend a sequence as far as possible using the EST sequences discussed above A consensus DNA sequence was assembled relative to other EST sequences using phrap and repeated

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PCR primers (forward and reverse) were synthesized:

딿 reverse PCR primer (40630-11) 5'-CAGAGCAGTGGATGTTCCCCCTGGG-3' (SEQ ID NO:380) forward PCR primer (40630_f1). 5'-CTGCCTCCACTGCTGTGCTGGG-3' (SEQ ID NO:379) Additionally, a synthetic oligonuclectide hybridization probe was constructed from the consensus DNA40630

sequence which had the following nucleotide sequence

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hybridization probe (40630.p1)

5'-CTGAACAAGATGGTCAAGCAAGTGACTGGGAAAAATGCCCCATCCTC-3' (SEQ ID NO;381)

for construction of the cDNA libraries was isolated from human breast tumor tissue. isolate clones encoding the PRO1561 gene using the probe oligonucleotide and one of the PCR primers. RNA screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

PRO1561 (designated herein as DNA76538-1670 [Figure 221, SEQ ID NO:377]; and the derived protein DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

sequence for PRO1561

ᄄ 5 signal peptide from about amino acid I to about amino acid 17, a transmembrane domain from about amino acid DNA 76538-1670 contains a single open reading frame with an apparent translational initiation site at nucleotide potential N-myristolation sites from about amino acid 20 to about amino acid 25 and from about amino acid 45 l to about amino acid 24, a potential N-glycosylation site from about amino acid 86 to about amino acid 89, 222 has an estimated molecular weight of about 12,910 daltons and a pl of about 6.41. Analysis of the fullpositions 29-31 and ending at the stop codon at nucleotide positions 377-379 (Figure 221). The predicted length PRO1561 sequence shown in Figure 222 (SEQ ID NO:378) evidences the presence of the following: a polypeptide precursor is 116 amino acids long (Figure 222). The full-length PRO1561 protein shown in Figure The entire nucleotide sequence of DNA76538-1670 is shown in Figure 221 (SEQ ID NO:377). Clone

20 acid 70. Clone DNA 76538-1670 has been deposited with ATCC on October 6, 1998 and is assigned ATCC to about amino acid 50 and a phospholipase A2 histidine active site from about amino acid 63 to about amino

ઇ PA2A_CRODU. P_R25416, P_R63055, P_P93363, P_R63046, PA2A_VIPAA, P_W58476, GEN13747, PA2X_HUMAN and bomology between the PRO1561 amino acid sequence and the following Dayhoff sequences: P_R63053, alignment analysis of the full-length sequence shown in Figure 222 (SEQ ID NO:378), evidenced significant An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

shown in Figure 221 (SEQ ID NO:377). was purchased and the insert obtained and sequenced, thereby giving rise to the DNA76538-1670 sequence DNA40630 consensus sequence and incyte EST clone no. 1921092. As such, Incyte EST clone no. 1921092 In addition to the above, a sequence homology search evidenced significant homology between the

EXAMPLE 115: Isolation of cDNA clones Encoding Human PRO1567

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33 (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater performed using the computer program BLAST or BLAST2 (Alishul of al., Methods in Enzymology databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database DNA47580. The DNA47580 sequence was then compared to a variety of expressed sequence tag (EST) A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated

that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green. University of Washington, Scattle, Washington). The consensus sequence obtained therrefrom is herein designated "DNA57246".

In light of the sequence homology between the DNA57246 sequence and EST no. 1793996 from the LIFESEQ[™] database, the clone containing the EST no. 1793996, which originates from a library constructed from prostate humor tissue, was purchased and the cDNA insert was obtained and sequenced. The sequence of this cDNA insert is shown in Figure 223 (SEQ ID NO:382) and is herein designated as DNA76541-1675.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 109-111, and a stop signal at nucleotide positions 643-645 (Fig. 223; SEQ ID NO:382). The predicted polypeptide precursor is 178 amino acids long has a calculated molecular weight of approximately 19,600 dations and an estimated p1 of approximately 5.89. Additional features include a signal peptide at about amino acids 1-22; a potential N-glycosylation site at about amino acids 1-727; a protein kinase C phosphorylation site at about amino acids 107-109; and potential N-myristoylation sites at about amino acids 46-51, 72-77, and 120-125.

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An analysis of the Dayboff database (version 35.45 SwissProx 35), using a WU-BLAST2 sequence sligument analysis of the full-length sequence shown in Figure 224 (SEQ ID NO:383), evidenced significant homology between the PRO1567 amino acid sequence and human colon specific gene CSG6 polypeptide designated Dayboff sequence "P_W06549". Homology was also found between the PRO1567 amino acid sequence and the following additional Dayboff sequences: HUAC002301_1, P_246880, A49685, SPBP_RAT, S42924, SPBP_MOUSE, 152115, MMU03711_1, and AF041468_31.

20 Clone DNA76541-1675 has been deposited with the ATCC on October 27, 1998, and is assigned ATCC deposit no. 203409.

EXAMPLE 116: Isolation of cDNA clones Encoding Human PRO1693

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described
25 in Example 1 above. This consensus sequence is herein designated DNA38251. Based on the DNA38251

contensus sequence, oligomacleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1693.

PCR primers (forward and reverse) were synthesized:

- 30 Interest PCR primer (18551.11) 5'-CTGGGATCTGAACAGTTTCCGGGC-3' (SEQ ID NO:386)

 reverse PCR primer (18551.11) 5'-GGTCCCCAGGACATGGTCTGTCCC-3' (SEQ ID NO:387)

 Additionally, a symbetic oligonucleotide bybridization probe was constructed from the consensus DNA38251 sequence which had the following nucleotide sequence

 hybridization probe (18531.611)
- 35 3'-GCTGAGTTTACATTTACGGTCTAACTCCCTGAGAACCATCCCTGTGCG-3' (SEQ ID NO:388)
 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to

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isolate clonus encoding the PRO1693 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1693 (designated herein as DNA77301-1708 [Figure 225, SEQ ID NO:384]; and the derived protein sequence for PRO1693.

20 15 5 length PRO1693 sequence shown in Figure 226 (SEQ ID NO:383) evidences the presence of the following: a deposited with ATCC on October 27, 1998 and is assigned ATCC deposit no. 203407. phosphorylation site from about amino acid 465 to about amino acid 468, a tyrosine kinase phosphorylation site about amino acid 250, from about amino acid 332 to ahout amino acid 337, from about amino acid 497 to about 11 to about amino acid 16, from about amino acid 33 to about amino acid 38, from about amino acid 245 to amino acid 502 and from about amino acid 507 to about amino acid 512. Clone DNA77301-1708 has been from about amino acid 136 to about amino acid 142 and potential N-mytistolation sites from about amino acid from about amino acid 504 to about amino acid 507, a cAMP- and cGMP-dependent protein kinase from about amino acid 357 to about amino acid 360, from about amino acid 496 to about amino acid 499 and 420 to about amino acid 442, potential N-glycosylation sites from about ammo acid 126 to about amino acid 129, signal peptide from about amino acid 1 to about amino acid 33, a transmembrane domain from about amino acid 226 has an estimated molecular weight of about 58,266 daltons and a pI of about 9.84. Analysis of the fullpolypeptide precursor is 513 amino acids long (Figure 226). The full-length PRO1693 protein shown in Figure positions 508-510 and ending at the stop codon at nucleotide positions 2047-2049 (Figure 225). The predicted DNA77301-1708 contains a single open reading frame with an apparent translational initiation site at nucleotide The entire nucleotide sequence of DNA77301-1708 is shown in Figure 225 (SEQ ID NO:384). Clare

An analysis of the Dayhoff database (version 33.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 226 (SEQ ID NO:385), evidenced significant homology between the PRO1693 amino acid sequence and the following Dayhoff sequences: AB071876_1, ALS_MOUSE, HSCHON03_1, P_R85889, AF062006_1. AB014462_1. A58532, MUSLRRPA_1, AB007865_1 and AF030435_1.

EXAMPLE 112: Isolation of cDNA clones Encoding Human PRO1784

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A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA43862. Based on the DNA43862 sequence, oligonucleotide probes were generated and used to screen a 30 human fetal kidney library prepared as described in paragraph I above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfI site; see, Holmes et al., Science, 233:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

forward PCR primer (ft) 5'-CTTTTCAGTGTCACCTCAGCGATCTC-3' (SEQ ID NO:391); and severe PCR primer (ft) 5'-CCAAAACATGGAGCAGGAACAGG-3' (SEQ ID NO:392).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA43862 sequence which had the following nucleotide sequence:

ybridization probe (p.)

5'-CCAGTTGGTGCTCTCGGACCTACCATGCGAAGAAGATGAAATGTGTG-3' (SEQ ID NO:393),

In order to acreen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clores encoding the PRO1784 gene using the probe oligonucleoside and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 68-70, and a stop signal at nucleotide positions 506-508 (Fig. 227; SEQID NO.389). The predicted polypeptide precursor is 146 amino acids long has a calculated molecular weight of approximately 16.116 daltons and an estimated pl of approximately 4.99. The approximate locations of the signal peptide, transmembrane domain and N-myristoylation site are indicated in Figure 228. Clone 10 DNA77303-2502 has been deposited with the ATCC and is assigned ATCC deposit no. 203479.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 228 (SEQ ID NO:390), evidenced sequence identity between the PRO1784 amino acid sequence and the following Dayhoff sequences: RNU87224_1, RNAF000114_1, P_W31947, S18038, AE001300_8, AF039833_1, P_W39833_1, P_W39788, HSU87223_1, NTU06712_1, and P_W31946.

EXAMPLE 118: Isolation of cDNA clones Encoding Human PRO1605

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A cDNA clone (DNA77648-1688) encoding a native human PRO160S polypeptide was identified by a years screen, in a human fetal kidney cDNA library that preferentially represents the 5' cods of the primary cDNA clones.

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The full-length DNA77648-1688 clone shown in Figure 229 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 425-427 and ending at the stop codon at nucleotide positions 845-847 (Filgure 229). The predicted polypeptide precursor is 140 amino acids long (Figure 230). The full-length PRO1605 protein shown in Figure 230 has an estimated molecular weight of about 15,668 daltons and a pl of about 10.14. Analysis of the full-length PRO1605 sequence shown in Figure 230 (SEQ ID NO:395) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 26. Clone DNA77648-1688 has been deposited with ATCC on October 27, 1998 and is assigned ATCC deposit no.

25

An analysis of the Dayhoff dambase (version 35.45 SwissProt 35), using a WU-BLAST2 sequence 30 alignment smalysis of the full-length sequence shown in Figure 230 (SEQ ID NO:395), evidenced algnificant bomology between the PRO1605 amino acid sequence and the following Dayhoff sequences: GNT5_HUMAN, P_R48975, P_W22519, MM26SPROT_1, HSU86782_1, CH60_LEPIN, HMCT_HELPY, F63126, HIU08875_1 and P_R41724.

35 EXAMPLE 119: Isolation of cDNA clones Encoding Human PRO1788

The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST

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duabases included public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ*, Incyte Pharmaccuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST? (Absobul et al., Methods in Enaymology, 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Incyte Clone No. 2968304 was identified as a sequence of interest having a BLAST score of 70 or greater that did not encode known proteins. The nucleotide sequence of heyre Clone No. 2968304 is designated herein as "DNA6612".

In addition, the DNA6612 sequence was extended using repeated cycles of BLAST and phrap (Phil Green, University of Washington, Seartle, Washington) to extend the sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is designated herein as "DNA49648". Based on the DNA49648 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1788.

PCR primers (forward and reverse) were synthesized:

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forward PCR primer: CCCTGCCAGCCGAGAGCTTCACC (49648.f1; SEQ ID NO:398)

teverse PCR primer: GGTTGGTGCCCGAAAGGTCCAGC (49648.rl; SEQ ID NO:399)

15 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA49648 sequence which had the following nucleotide sequence:

<u>brbridiaaisngmbe</u>: CAACCCCAAGCTTAACTGGGCAGGAGCTGAGGTGTTTTCAGGCQ49648.p1; SEQ ID NO:400)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was 20 screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1788 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1788 (designated herein as DNA77652-2505 [Figure 231, SEQ ID NO:396]; and the derived protein sequence for PRO1788.

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The entire coding sequence of PRO1788 is shown in Figure 231 (SEQ ID NO:396). Clone DNA77652-2505 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 64-66 and an apparent stop codon at nucleotide positions 1123-1125. The predicted polypeptide precursor is 333 armino solds long. The full-length PRO1788 protein shown in Figure 232 has an estimated molecular weight of

- 30 about 37,847 dations and a pl of about 6.80. Additional features of PRO1788 include: a signal peptide at about amino acids 1-16; transmembrane domains at about amino acids 215-232 and 287-304; potential N-glycosylation sites at about amino acids 74-77 and 137-140; a glycosymninoglycan attachment site at about amino acids 45-48; a tyrotine kinase phosphorylation site at about amino acids 318-325; N-myristoylation sites at about amino acids 11-18, 32-37, 88-93, 214-219, and 223-228; and a leucine zipper pattern at about amino acids 284-305.
- 35 An analysis of the Dayboff database (version 35.45 SwissProt 35), using a WU-BLAST? sequence alignment analysis of the full-length sequence shown in Figure 232 (SEQ ID NO:397), revealed significant homology between the PRO1788 amino acid sequence and the following Dayboff sequences: AF030435_1;

AP062006_1; DMTARTAN_1; GARP_HUMAN; 542799; P_R71294; HSU88879_1; DROWHEBLER_1: AS8532: عنط AP068920_1.

Clone DNA77652-2505 was deposited with the ATCC on November 17, 1998, and is assigned ATCC posit no. 203480.

EXAMPLE 120: Isolation of cDNA clones Encoding Human PRO1801

A proprietary expressed sequence use (EST) DNA database (LIFESEQ**, heyre Pharmaceuticals, Palo Alto, CA) was starched and an EST was identified which showed homology to the IL-19 protein. This EST sequence is Incyte EST clone no. 819592 and is herein designated DNA79293. Based on the DNA79293 sequence, oligonucleosides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1801.

PCR primers (forward and reverse) were synthesized:

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PCR primer 5'-GTCCTGTGGTCTCCAGATTTCAGGCCTA-3' (SEQ ID NO:403)

PCR primer 5'-AGTCCTCCTTAAGATTCTGATGTCAA-3' (SEQ ID NO:404)

RNA for construction of the cDNA libraries was isolated from human fetal kidney issue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a Notl site. linked with blunt to Sall hemikinased adaptors, cleaved with Notl, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRKSB is a precursor of pRKSD that does not contain the Sfil site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique Xhol and Notl sites.

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DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1801 (designated herein as DNA83500-2506 [Figure 233, SEQ ID NO:401]; and the derived protein sequence for PRO1801.

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The entire nucleotide requence of DNA83500-2506 is shown in Figure 233 (SEQ ID NO:401). Clone

25 DNA83500-2506 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 109-111 and ending at the stop codon at nucleotide positions 892-894 (Figure 233). The predicted polypoptide precursor is 261 amino acids long (Figure 234). The full-length PRO1801 protein shown in Figure 234 has an estimated molecular weight of about 29,667 daltons and a pl of about 8.76. Analysis of the full-length PRO1801 equence shown in Figure 234 (SEQ ID NO:402) evidences the presence of the following: a 30 signal peptide from about amino acid 10 about amino acid 42, cAMP- and cGMP-dependent protein kinase phosphorylation sites from about amino acid 192 to about amino acid 195 and from about amino acid 225 to

30 signal peptide from about amino acid 1 to about amino acid 42, cAMP- and cGMP-dependent protein kinase phosphorylation sites from about amino acid 192 to about amino acid 192 and from about amino acid 225 to about amino acid 228 and potential N-myristolation sites from about amino acid 42 to about amino acid 47, from about amino acid 46 to about amino acid 51 and from about amino acid 42 to about amino acid 41. Clone DNA83500-2506 has been deposited with ATCC on October 29, 1998 and is assigned ATCC deposit no. 35 203391.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST? sequence alignment analysis of the full-length sequence shown in Figure 224 (SEQ ID NO:402), evidenced significant

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homology between the PRO1801 amino acid sequence and the following Dayhoff sequences: P_W37935. HGS_B477, P_R32277, IL10_MACFA, P_W46585, P_R39714, P_R71471, P_R10159, IL10_RAT and P_W57201.

EXAMPLE 121: Isolation of cDNA clones Encoding Human UCP4

EST databases, which included public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQT^M, Incyte Pharmaceuticals, Palo Alto, CA), were searched for sequences having homologies to human UCP3. The search was performed using the computer program BLAST or BLAST2 [Altschul et al., <u>McMods in Eurymology</u>, 266:460-480 (1996)] as a comparison of the UCP3 protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater 10 that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program AssemblLIGN and MacVector (Oxford Molecular Group, Inc.).

A DNA sequence ("fromDNA") was assembled relative to other EST sequences using AssemblLIGN software. In addition, the fromDNA sequence was extended using repeated cycles of BLAST and AssemblLIGN to extend the sequence as far as possible using the sources of EST sequences discussed above. Based on this DNA sequence, oligomucleotides were synthesized to isolate a clone of the full-length coding sequences for UCP4 by PCR. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligomucleotides are synthesized when the consensus sequence is greater

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20 PCR primers (forward and reverse) were synthesized:

than about 1-1.5kbp.

forward PCR primer CGCGGATCCCGTTATCGTCTTGCGCTACTGC (SEQ ID NO:407)

rewerse PCR primer GCGGAATTCTTAAAATGGACTGACTCCACTCATC (SEQ ID NO:408)

RNA for construction of the cDNA libraries was isolated from brain tissue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such 25 as those from invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a Notl site, linked with blunt to Sall hemikinased adaptors, cleaved with Notl, sized appropriately by get electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRKSB is a precursor of pRKSD that does not contain the Sfil site; see, Holmes et al., <u>Sclence</u>, 253:1278-1280 (1991)) in the unique Xhol and Notl sites.

30 DNA sequencing of the clone isolated by PCR as described above gave the full-length DNA sequence for UCP4 (designated herein as DNA77568-1626 [Figure 235, SEQ ID NO:405] and the derived proxein sequence for UCP4.

The entire coding sequence of UCP4 is shown in Figure 235 (SEQ ID NO:405). Close DNA775681626 contains a single open reading frame with an apparent translational initiation site at undetotide positions
35 27-29, and an apparent stop codon at nucleotide positions 996-998. (See Figure 235; SEQ ID NO:405). The
predicted polypeptide precursor is 323 amino acids long. It is presently believed that UCP4 is a membranebound protein and commins at least 6 transmembrane regions. These putative transmembrane regions in the

molecular weight of about 36,061 daltons and a pl of about 9.28. approximate 972 plus 34 bp insert. The full-length UCP4 protein shown in Figure 236 has an estimated ATCC 203134 vector. Digestion of the vector with BamHI and BeoRI restriction enzymes will yield an polypoptide is obtained or obtainable by expressing the molecule encoded by the cDNA insert of the deposited vector (Invitrogen) has been deposited with ATCC and is assigned ATCC deposit no. 203134. UCP4 UCP4 amino acid sequence are illustrated in Figure 236. Clone DNA77568-1626, contained in the pcDNA3

EXAMPLE 122: Isolation of cDNA clones Encoding Human PRO193

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PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the in Example 1 above. Based on this consensus sequence, oligonucleotides were synthesized: 1) to identify by full-length coding sequence for PRO193. A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

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A pair of PCR primers (forward and reverse) were synthesized:

5'-GTTTGAGGAAGCTGGGATAC-3' (SEQ ID NO:411); and

reverse PCR primer 5'-CCAAACTCGAGCACCTGTTC-3' (SEQ ID NO:412).

5 had the following nucleotide sequence: Additionally, a synthetic oligonucleoride hybridization probe was constructed from the consensus sequence which

5'-ATOGCAGGCTTCCTAGATAATTTTCGTTGGCCAGAATGTG-3' (SEQ ID NO:413).

20 screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to for construction of the cDNA libraries was isolated from human retina tissue (LIB94). isolate clones encoding the PRO193 gene using the probe oligonucleotide and one of the PCR primers. RNA In order to server a libraries for a source of a full-length clone, DNA from the libraries was

PRO193 [herein designated as DNA23322-1393] (SEQ ID NO:409) and the derived protein sequence for DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

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DNA23322-1393 contains a single open reading frame with an apparent translational initiation site at nucleotide polypeptide precursor is 158 amino acids long (Figure 238). The full-length PRO193 protein shown in Figure positions 138-140 and ending at the stop codon at nucleotide positions 612-614 (Figure 237). The predicted The entire nucleotide sequence of DNA23322-1393 is shown in Figure 237 (SEQ ID NO:409). Close

ಜ 238 has an estimated molecular weight of about 17,936 and a pl of about 5.32. Clone DNA23322-1393 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correst sequence, and the sequences provided herein are based on known sequencing techniques.

35 81-83 of SEQ ID NO:410. A peroxidase proximal heme-ligand domain is at about amino acids 81-83 of SEQ ID NO:410. The corresponding nucleotides can be routinely determined given the sequences provided herein. acids 23-42, 60-80, 97-117 and 128-148 of SEQ ID NO:410. A cell attachment sequence is at about amino acids Still analyzing the amino acid sequence of SEQ ID NO:410, transmembrane domains are at about amino

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EXAMPLE 123: Isolation of cDNA clones Encoding Human PRO1130

in Example 1 above. This consensus sequence is herein designated DNA34360. Based on the DNA34360 the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

PCR primers (forward and reverse) were synthesized:

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STANT PCR primer (34360.11) 5'-GCCATAGTCACGACATGGATG-3' (SEQ ID NO:416) orward PCR primer (34360,12) 5'-GGATGGCCAGAGCTGCTG-3' (SEQ ID NO:417)

ö Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA34360 reverse PCR primer (34360.r1) sequence which had the following nucleotide sequence REVERSE_PCR_printer (34360.12) 5'-ATTCTCTCCACAGACAGCTGGTTC'3' (SEQ ID NO:420) forward PCR primer (34360.f1) S'-AAAGTACAAGTOTGGCCTCATCAAGC-3' (SEQ ID NO:418) 5'-TCTGACTCCTAAGTCAGGCAGGAG-3' (SEQ ID NO:419)

hybridization probe (34360.p1)

2 5'-GTACAAGTGTGGCCTCATCAAGCCCTGCCCAGCCAACTACTTTGCG-3' (SEQ ID NO:421)

for construction of the cDNA libraries was isolated from human aortic endothelial cell tissue. screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1130 gene using the probe oligonucleotide and one of the PCR primers. RNA In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

20 PRO1130 (designated herein as DNA59814-1486 [Figure 239, SEQ ID NO:414]; and the derived protein sequence for PRO1130. DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

25 kngth PRO1130 sequence shown in Figure 240 (SEQ ID NO:415) evidences the presence of the following: a polypeptide precursor is 224 amino acids long (Figure 240). The full-length PRO1130 protein shown in Figure positions 312-314 and ending at the stop codon at nucleotide positions 984-986 (Figure 239). The predicted DNA59814-1486 contains a single open reading frame with an apparent translational initiation site at nucleotide 240 has an estimated molecular weight of about 24,963 daltons and a pl of about 9.64. Analysis of the full-The entire nucleotide sequence of DNA59814-1486 is shown in Figure 239 (SEQ ID NO:414). Clone

30 ATCC deposit no. 203359. amino acid 184 to about amino acid 191 and a potential N-glycosylation site from about amino acid 107 to about amino acid 110. Clone DNAS9814-1486 has been deposited with ATCC on October 20,1998 and is assigned signal peptide from about amino acid I to about amino acid 15, an ATP/GTP-binding site motif A from about

homology between the PRO1130 amino acid sequence and the following Dayhoff sequences: P_W06547 lignment analysis of the full-length sequence shown in Figure 240 (SEQ ID NO:415), evidenced significant An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence

ઝ 216_HUMAN, D87120_1, MMU72677_1, LAU04889_1, and D69319.

EXAMPLE 124: Isolation of cDNA clones Encoding Human PRO1335.

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA35727. Based on the DNA35727 consensus sequence oligonucleotides were symbosized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1335.

PCR primers (forward and reverse) were synthesized:

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Security PCR primer (35727.f1) 5'-GTAAAGTCGCTGGCCAGC:3' (SEQ ID NO:424)

IONWARD PCR primer (35727.12) 5'-CCCGATCTGCCTGCTGTA-3' (SEQ ID NO:425)

TEVERSE PCR primer (35727.41) 5'-CTGCACTGTATGGCCCATTATTGTG-3' (SEQ ID NO:426)

10 Additionally, a synthetic oligonucleoside hybridization probe was constructed from the consensus DNA35727 requence which had the following nucleotide sequence

hybridization probe (33727.p1)

5'-CAGAAACCCATGATACCCTACTGAACACCGAATCCCCTGGAAGCC-3' (SEQ ID NO;427)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1335 gene using the probe oligonucleoxide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human retina tissue.

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DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1335 (designated herein as DNA62812-1594 [Figure 241, SEQ ID NO:422]; and the derived protein sequence for PRO1335.

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The entire nucleoxide sequence of DNA62812-1594 is shown in Figure 241 (SEQ ID NO:422). Clone DNA62812-1594 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 271-273 and ending at the stop codon at nucleotide positions 1282-1284 (Figure 241). The predicted polypeptide precursor is 337 amino acids long (Figure 242). The full-length PRO1335 protein shown in Figure 242 has an estimated molecular weight of about 37,668 daltons and a pl of about 6.27. Analysis of the full-length PRO1335 sequence shown in Figure 242 (SEQ ID NO:423) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 1 to about amino acid 213 to about amino acid 216 and amino acid 310, a priemial N-glycosylation site from about amino acid 213 to about amino acid 251, from about amino acid 104 to about amino acid 140 and from about amino acid 25 to about amino acid 265. Clone DNA62812-1594 has been deposited with ATCCC on September

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9, 1998 and is assigned ATCC deposit no. 203248.

An analysis of the Dayholf database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 242 (SEQ ID NO:423), evidenced significant 35 homology between the PRO1335 amino acid sequence and the following Dayholf sequences: AF037335_1, 138013, PTPG_MOUSE, CAH2_HUMAN, ICAC, CAH7_HUMAN, CAH3_HUMAN, CAH1_HUMAN, CAH5_IUMAN and P_K41746.

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EXAMPLE 125: Isolation of cDNA clones Encoding Human PRO1329

Use of the signal sequence algorithm described in Example 3 above allowed idemification of an EST cluster sequence from the LIFESEQ® database, designated Incyte Cluster No. 167344, also referred herein as "DNA 10880". This EST cluster sequence was then compared to a variety of expressed sequence uag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmacentrials, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Alishul et al., Methods in Enzymology 285:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a comsensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was derived from a CDNA library constructed from RNA isolated from synovial membrane tissue removed from the elbow of a female with rheumatoid arthritis. The construsts sequence obtained therefrom is herein designated "DNA88836".

In light of the sequence homology between the DNA58836 sequence and a sequence contained within the Incyte EST clone no. 368774, EST clone 368774 was purchased and the cDNA insert was obtained and 15 sequenced. The sequence of this cDNA insert is shown in Figure 243 and is herein designated as DNA66666-1585.

The full length clone shown in Figure 243 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 90 to 92 and ending at the stop codon found at nucleotide positions 717 to 719 (Figure 243; SEQ ID NO:428). The predicted polypeptide precursor (Figure 244, SEQ 20 ID NO:429) is 209 amino acids long, with a signal sequence at about amino acids 1-16. PRO1329 has a calculated molecular weight of approximately 21,588 dations and an estimated p1 of approximately 5.50. Clone DNA66660-1585 was deposited with the ATCC on September 22, 1998 and is assigned ATCC deposit no. 203279.

An analysis of the Dayboff database (version 35,45 SwissPon 35), using a WU-BLAST2 sequence
25 alignment analysis of the full-length sequence abown in Figure 244 (SBQ ID NO:429), revealed some homology
between the PRO1329 amino acid sequence and the following Dayboff sequences: CELX06A9_3
PROA_XANCP, CXU21300_4, MTV037_17, SYN1_RAT, 156542, 560743, BNOLE3_1, AB001573_1, and
P PROA_

30 EXAMPLE 126: Isolation of cDNA clones Encoding Human PRO1550

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST sequence from the Merck database, designated CELT15B7_12, also referred herein as "DNA10022". This EST sequence was then compared to a variety of expressed sequence tag (EST) databases which included public and proprietary EST databases (e.g., GenBank and LIFESEQ*) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST3 (Altabal et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and astembled imo a conseasus DNA sequence with the

program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated "DNASS708".

In light of the sequence homology between the DNASS708 sequence and a sequence contained within Incyre EST no. 3411659, the EST clone 3411659 was purchased and the cDNA insert was obtained and sequenced in its entirety. The sequence of this cDNA insert is shown in Figure 245 and is berein designated as "DNA76393-1664".

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The full length clone shown in Figure 245 comained a single open reading frame with an apparent translational initiation site at nucleotide positions 138 to 140 and ending at the stop codon found at nucleotide positions 867 to 869 (Figure 245; SEQ ID NO:430). The predicted polypeptide precursor (Figure 246, SEQ ID NO:431) is 243 amino acids long. Other features of the PRO1550 protein include: a signal sequence at about amino acids 1-30; a hydrophobic domain at about amino acids 195-217; and a potential N-glycoxylation site at about amino acids 186-189. PRO1550 has a calculated molecular weight of approximately 26,266 daltons and an estimated pl of approximately 8.43. Clone DNA76393-1664 was deposited with the ATCC on October 6, 1998, and is assigned ATCC deposit no. 203323.

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An analysis of the Dayhoff database (version 33.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 246 (SEQ ID NO:431), revealed some homology between the PRO1550 amino acid sequence and the following Dayhoff sequences: CELF59E12_11; CA24_ASCSU; AF018082_1; CA13_BOVIN: CA54_HUMAN: CA34_HUMAN; HUMCOL7A1X_1; P_W09643; AF053538_1; and HSEMCXIV2_1.

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20 EXAMPLE 127: Use of PRO as a hybridization probe.

The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

DNA comprising the coding sequence of full-length or manure PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue genomic libraries.

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Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8. 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

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EXAMPLE 128: Expression of PRO in E. coli

This example littstrates preparation of an unglycosylated form of PRO by recombinant expression in E. coti.

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The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected

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expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from E. coli: see Bolivar et al., Gene. 2:95 (1977)) which comains genes for ampicillin and ettracycline resistance. The vector is digested with restriction crayme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trip promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, hambda transcriptional terminator, and an arell sene.

The ligation mixture is then used to transform a selected *E. culi* strain using the methods described in Sambrook et al., 20072. Transformants are identified by their ability to grow on LB plates and ambitotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

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Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with annibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell 15 pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

30 25 20 pellets are frozen until purification and refolding yeast extract, 5.36 g Sheffield hyease SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) CRAP media (prepared by mixing 3.57 g (NH₄)₂SO₄, 0.71 g sodium cirate*2H2O, 1.07 g KCl, 5.36 g Difco carbenicillin at 30°C with shaking until an O.D. 600 of 3-5 is reached. Cultures are then diluted 50-100 fold into fuhA(tonA) lon galE rpolfis(htpRts) clpP(laclq). Transforments are first grown in LB containing 50 mg/ml sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful encoding PRO is initially amplified using selected PCR primers. The primers will commin restriction enzyme glucose and 7 mM MgSO.) and grown for approximately 20-30 hours at 30°C with shaking. Samples are ligated into an expression vector, which is used to transform an E. coll host based on strain 52 (W3110 column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell PRO may be expressed in $E.\ coli$ in a poly-His tagged form, using the following procedure. The DNA

E. coll paste from 0.3 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guankline, 20 mM Tris, pH 8 buffer. Solid sodium suffice and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sufficilization. The solution is centrifuged at 40,000 35 ppm in a Beckman Ultracentifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guaridine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qingen Ni-NTA metal chelate column equilibrated in the metal chelate.

column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbitchem, Utrol grade), pH 7.4. The protein is cluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

15 10 s of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and I mM EDTA reversed phase resin. Aggregated species are usually cluted at higher acctorainile concentrations. In addition refolded protein is chromatographed on a Poros RI/H reversed phase column using a mobile buffer of 0.1% solution is filtered through a 0.22 micron filter and acctonitrile is added to 2.10% final concentration. The to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the since those species are the most compact with their hydrophobic interiors shielded from interaction with the Generally, the properly refolded species of most proteins are cluted at the lowest concentrations of acetonitrile TFA with ebriton with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is quenched by the addition The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting

Fractions containing the desired folded PRO polypeptide are pooled and the accionitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium ethoride and 4% mannitol by dialysis or by get filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

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Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 129: Expression of PRO in mammalian cells

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This example illustrates preparation of a potentially glycoxylated form of PRO by recombinant expression in mammalian cells.

The vector, pRKS (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRKS with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., <u>supra</u>. The resulting vector is called pRKS PRO.

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In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, murient components and/or antibiotics. About 10 µg pRKS-PRO DNA is mixed with about 1 µg DNA encoding the VA RNA gene [Thismasppaya et al., Cell, 21:543 (1982)] and dissolved in 500 µl of 1 mM DNA encoding the VA RNA gene [Thismasppaya et al., Cell, 21:543 (1982)] and dissolved in 500 µl of 150 mM HEPES (pH Tris-HCl, 0.1 mM EDTA, 0.227 M CaCl₃. To this mixture is added, dropwise, 500 µl of 59 mM HEPES (pH T.35), 280 mM NaCl, 1.5 mM NaPO_n, and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The

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culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200 μCi/ml ¹⁸S-cysteine and 200 μCi/ml ¹⁸S-methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS get. The processed get may be dried and exposed to film for a selected period of time to reveal the

presence of PRO polypepide. The cultures containing transfercted cells may undergo further incubation (in serum free medium) and the medium is rested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulface method described by Sompanyrae et al., <u>Proc. Natl. Acad. Sci.</u> 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 µg pRKS-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 µg/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any aclosted method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRKS-PRO can be transfected into CHO cells using known reagents such as CaPO, or DEAE-dextran. As described above, the cell cultures can be incribated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as 20 MS-methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incribated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the PRO may be subcloned out of the PRO may be subcloned out of the PRO may be subcloned insert can undergo PCR to fase in frame with a selected epitope tag such as a polyhis tagged PRO insert can then be subcloned into a \$V40 driven vector containing a selection marker such as DHPR for selection of stable clones. Finally, the CHO cells can be transferred (as described above) with the \$V40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by Ni¹²-chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoathesin), in which the coding sequences for the soluble forms (e.g. extracellular 35 domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloped in a CHO expression vector using

standard techniques as described in Ausubel et al., <u>Current Protocols of Molecular Biology</u>. Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., <u>Nucl. Acids Res.</u> 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductate (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transferien.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect* (Quiagen), Dosper* or Fugenz* (Bochringer Mannheim). The cells are grown as described in Lucas et al., <u>sprg.</u> Approximately 3 x 10.7 cells are frozen in an ampule for further growth and production as described below.

25 20 5 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL stored at 4°C or immediately loaded onto columns for purification. the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below polydimethylsiloxane emultion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35%) 70%, the cell culture is harvested by centrifugation and filtering through a 0.22 $\,\mu{\rm m}$ filter. The filtrate was either 3L production spinner is seeded at 1.2 x 10° cells/mL. On day 0, the cell number pH ie determined. On day a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A μm filtered PS20 with 5 % 0.2 μm diafiltered fetal bovinc scrum). The cells are then aliquoted into a 100 mL centrifugation and resuspension in production medium. Although any suitable CHO media may be employed and 2000 mL spinners are seeded with 3 x 10° cells/mL. The cell media is exchanged with fresh media by spianer containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2 vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by

For the poly-His neged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4.5 ml/min, at 4°C. After loading, the column is washed with additional equilibration buffer and the protein cluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% manniol, pH 6.8, with a 25 ml G25 Superfine (Pharimacia) column and stored at -80°C.

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Immunoadhesin (Fe-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column to washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The cluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275 µL of 1 M Tris buffer, pH 9. The highly purified protein is subsequently

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desalted imo storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gets and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 130: Expression of PRO in Yeast

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The following method describes recombinant expression of PRO in yeast

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding PRO can be clored into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertage secretory

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in solected fermentation media. The transformed yeast supermanns can be analyzed by precipitation with 10% trichloroacciic acid and separation by SDS-PAGE, followed by staining of the gets with

signal/leader sequence, and linker sequences (if needed) for expression of PRO.

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Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate commaning PRO may further be purified using selected column chromatography resides.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 131: Expression of PRO in Baculovirus-Infected Insect Cells

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The following method describes recombinant expression of PRO in Baculovirus-infected inect cells.

The sequence cooling for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-this tags and immunoglobulin tags (like Fc regions of 1gO).

25 A variety of plasmids may be employed, including plasmids derived from commercialty available plasmids such as PVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the manure protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flunking (selected) restriction enzyme sites. The product 30 is then digested with those selected restriction enzymes and subcloned into the extraction vector.

30 is then digested with those selected restriction enzymes and subclossed into the expression vector.
Recombinant baculovirus is generated by co-transferting the above plasmid and BaculoGoldTM virus
DNA (Pharmingen) into Spadoptera fragiperata (*SP9*) cells (ATCC CRL 1711) using lipofectin (commercially

DNA (Pharmingen) into Spodoptera fragiperda (*S9*) cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et 3.5 al., Basalovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

Expressed poly-his tagged PRO can then be purified, for example, by Ni²-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by

Rupert et al., Nature, 352:175-179 (1993). Briefly, S/9 cells are washed, resuspended in sonication buffer (25 ml. Hepes, pH 7.9; 12.5 ml MgCl₃; 0.1 ml EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 ml phosphate, 300 ml NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 µm filter. A Ni²⁺-NTA agarose column (commercially available from Qlagen) is prepared with a bed volume of 5 ml, washed with 25 ml of water and equilibrated with 25 ml of loading buffer. The filtered cell extract is loaded outo the column at 0.5 ml, per minute. The column is washed to baseline A₁₀₀ with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 ml phosphate; 300 ml NaCl, 10% glycerol, pH 6.0), which clutes nonspecifically bound protein. After reaching A₁₀₀ baseline again, the column is developed with a 0 to 500 ml Indiazole gradient in the secondary wash buffer. One ml fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with Ni²⁺-NTA-conjugated to alkaline phosphatuse (Qiagen). Fractions containing the cluted His₁₀-tagged PRO are pooled and dialyzed against loading buffer.

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Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

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EXAMPLE 132: Preparation of Antibodies that Bind PRO

This example illustrates preparation of monoclonal antibodies which can specifically bind PRO

Techniques for producing the monoclonal amihodies are known in the art and are described, for 20 instance, in Goding, sugra, Immunogens that may be employed include purified PRO, fusion proteins comaining PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Bable, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected auboutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, 25 the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emultified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO amibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell time such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, uninopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of Postitive hybridoma cells secreting the destred monoclonal antibodies against PRO is within the skill in the art. ž

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The positive hybridoma cells can be injected intrapertioneally into syngenetic Bable mice to produce ascites containing the anti-PRO monoclonal authodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antihodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antihody to protein A or protein G can be employed.

EXAMPLE 133: Parification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the art of protein purification. For example, pro-PRO polypeptide, manure PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to

an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscasaway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoclohulin is covalently attached to a

15 chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE™ (Pharmacia LKB Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction 20 from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypepide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (e.g., high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (e.g., a low pH buffer such as approximately pH2.3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

30 EXAMPLE 134: Drug Screening

This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukanyotic or prokaryotic host cells which are stably 35 transformed with recombinant medicic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, cam be used for sundard binding assays. One may measure, for example, the formation of complexes between PRO

polypeptide or a fragment and the agent being texted. Alternatively, one can examine the diminution in complet formation between the PRO polypeptide and its target cell or ranger receptors caused by the agent being texted.

Thus, the measure invasion and the agent being texted.

Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such as agent with an PRO polypeptide or fragment thereof and assaying (f) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984.

Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art.

15 Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening to comiques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of my peptide which shares one or more antigenic determinants with PRO polypeptide.

EXAMPLE 135: Rational Drug Design

The goal of raisonal drug design is to produce structural analogs of biologically active polypepide of interest (i.e., a PRO polypepide) or of small molecules with which they interact, e.g., agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypepide or which enhance or interfere with the function of the PRO polypepide in vivo (c.f., Hodgson, Biol/Icchanlogy, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to educidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda et al., L. Biochem., 113:742-746

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(1993).

and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to hypass protein crystallography altogether by generating ami-idioxypic amibodies (ami-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced peptides. The isolated

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide 10 amino acid sequence provided herein will provide guidance to those employing computer modelling techniques in place of or in addition to x-ray crystallography.

peptides would then act as the pharmacore.

Deposit of Material

The following materials have been deposited with the American Type Culture Collection, 1080;

15 University Blvd., Manassas. VA 20110-2209, USA (ATCC):

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DNA62808-1326	DNA61608-1606	DNA61185-1646	DNA60775-1532	DNA60764-1533	DNA60740-1615	DNA60618-1557	DNA60611-1524	DNA60608-1577	DNA60278-1530	DNA59817-1703	DNA59586-1520	DNA59219-1613	DNA59218-1559	DNA59212-1627	DNA58852-1637	DNA58828-1519	DNA58732-1650	DNA58730-1607	DNA58727-1474	DNA57841-1522	DNAS7254-1477	DNA56862-1343	DNA56531-1648	DNAS6529-1647	DNA56406-1704	DNA56107-1415	DNA26846-1397	DNA19902-1669	Material	
203358	203239	203464	203173	203452	203456	203292	203175	203126	203170	203470	203288	203220	203287	203245	203271	203172	203290	203221	203171	203458	203289	203174	203286	203293	203478	203405	203406	203454	ATCC Dep. No.	Table 2
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DNA6880-1676 DNA6888-1570 DNA71166-1685 DNA71160-1799 DNA71180-1653 DNA71180-1653 DNA71180-1653 DNA71181-1659 DNA71231-1659 DNA71232-1651 DNA7127-1656	DNA6672-1596 DNA66673-1597 DNA66673-1587 DNA66678-1649 DNA68836-1669 DNA68866-1644 DNA68866-1644 DNA6887-1628 DNA6887-1628	DNA6551-136 DNA65512-156 DNA65512-156 DNA66521-153 DNA66521-158 DNA6652-1616 DNA66638-1584 DNA6668-1593 DNA6668-1597	DNA654(2)-1506 DNA654(2)-1506 DNA654(2)-1507 DNA654(3)-1507 DNA654(3)-1507 DNA654(3)-1507 DNA654(3)-1507 DNA654(3)-1506 DNA654(3)-1506 DNA654(3)-1506 DNA654(3)-1506 DNA654(3)-1506	DNA64886-1601 DNA64888-1502 DNA64888-1542 DNA64888-1541 DNA64897-1628 DNA64907-1627 DNA64907-1553 DNA64907-1558 DNA64907-1580 DNA64907-1580	DNA62809-1531 DNA62845-1694 DNA62945-1694 DNA64942-1632 DNA64899-1609 DNA64891-1602 DNA64881-1602 DNA64881-1526 DNA64885-1526
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September 12, 1998 October 6, 1998 October 6, 1998 October 6, 1998 October 20, 1998 November 17, 1998 October 27, 1998 September 22, 1998 October 27, 1998 October 27, 1998 October 27, 1998 October 27, 1998 October 6, 1998	September 22, 1998 September 23, 1998 November 3, 1998 September 22, 1998 September 22, 1998 September 22, 1998 September 22, 1998	Ciciober 6, 1998 September 15, 1998 September 21, 1998 September 22, 1998 September 22, 1998	September 15, 1998 September 9, 1998 September 15, 1998 September 17, 1998 September 17, 1998 September 15, 1998	September 9, 1998 September 9, 1998 September 9, 1998 September 15, 1998 September 15, 1998 October 6, 1998 September 15, 1998 September 15, 1998 September 15, 1998	September 9, 1998 September 20, 1998 October 20, 1998 September 21, 1998 November 17, 1998 September 9, 1998 September 9, 1998 September 9, 1998 September 9, 1998 November 17, 1998

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DNA77568-1626 DNA23372-1393 DNA59814-1486 DNA65812-1594 DNA66660-1585 DNA76393-1664	DNA77301-1708 DNA77303-2502 DNA77648-1688 DNA77652-2505 DNA833500-2506	DNA76329-1666 DNA76331-1701 DNA76332-1702 DNA76338-1670 DNA76341-1675	DNA76398-1699 DNA76399-1700 DNA76401-1683 DNA76510-2504 DNA76522-2500	DNA73742-1662 DNA73744-1665 DNA73746-1654 DNA73760-1672 DNA73760-1698	DNA73734-1680 DNA73734-1681 DNA73735-1681 DNA73736-1657 DNA73737-1658 DNA73739-1645	DNA71286-1604 DNA71883-1660 DNA73401-1633 DNA73492-1671 DNA73772-1673 DNA73770-1679
203134 203400 203389 203248 203279 203273	203407 203479 203408 203480 203391	20315 203465 203473 203313 203409	203474 203472 203360 203477 203469	203316 203322 203411 203314 203471	203363 203363 203356 203466 203412 203270	203357 203475 203475 203273 203324 203459 203329
August 18, 1998 October 27, 1998 October 20, 1998 September 9, 1998 September 22, 1998 October 6, 1998	October 27, 1998 November 17, 1998 October 27, 1998 November 17, 1998 October 29, 1998	October 6, 1998 November 17, 1998 November 17, 1998 October 6, 1998 October 27, 1998	November 17, 1998 November 17, 1998 October 20, 1998 November 17, 1998 November 17, 1998	October 6, 1998 October 6, 1998 October 6, 1998 October 72, 1998 October 6, 1998 October 6, 1998	October 20, 1998 October 20, 1998 October 20, 1998 October 17, 1998 October 27, 1998 Sentember 27, 1998	Octuber 20, 1998 November 17, 1998 September 22, 1998 October 6, 1998 November 3, 1998

45 8 to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The USC §122 and the Commissioner's rules pursuant thereto (including 37 CFR §1.14 with particular reference to public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest 886 OG 638). between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of These deposit were made under the provisions of the Budapest Treaty on the International Recognition

50 notification with another of the same. Availability of the deposited material is not to be construed as a license die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on The assignee of the present application has agreed that if a culture of the materials on deposit should

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to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and full within the scope of the appended claims.

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WHAT IS CLAIMED IS:

35 30 ટ 20 15 0 NO:282), Figure 162 (SEQ ID NO:287), Figure 164 (SEQ ID NO:292), Figure 166 (SEQ ID NO:297), Figure NO: 146), Figure 92 (SEQ ID NO:148), Figure 94 (SEQ ID NO:153), Figure 96 (SEQ ID NO:158), Figure 98 NO:395), Figure 232 (SEQ ID NO:397), Figure 234 (SEQ ID NO:402), Figure 236 (SEQ ID NO:406), Figure 224 (SEQ ID NO:383), Figure 226 (SEQ ID NO:385), Figure 228 (SEQ ID NO:390), Figure 230 (SEQ ID 196 (SEQ ID NO:336), Figure 198 (SEQ ID NO:338), Figure 200 (SEQ ID NO:340), Figure 202 (SEQ ID 126 (SEQ ID NO:220), Figure 128 (SEQ ID NO:225), Figure 130 (SEQ ID NO:227), Figure 132 (SEQ ID 54 (SEQ ID NO:88), Figure 56 (SEQ ID NO:95), Figure 58 (SEQ ID NO:100), Figure 60 (SEQ ID NO:102) 16 (SEQ ID NO:24), Figure 18 (SEQ ID NO:29), Figure 20 (SEQ ID NO:31), Figure 22 (SEQ ID NO:33), NO:308), Figure 176 (SEQ ID NO:310), Figure 178 (SEQ ID NO:315), Figure 180 (SEQ ID NO:317), Figure NO:229), Figure 134 (SEQ ID NO:234), Figure 136 (SEQ ID NO:236), Figure 138 (SEQ ID NO:243), Figure (SEQ ID NO:160), Figure 100 (SEQ ID NO:162), Figure 102 (SEQ ID NO:170), Figure 104 (SEQ ID 238 (SEQ ID NO:410), Figure 240 (SEQ ID NO:415), Figure 242 (SEQ ID NO:423), Figure 244 (SEQ ID 210 (SEQ ID NO:358), Figure 212 (SEQ ID NO:364), Figure 214 (SEQ ID NO:366), Figure 216 (SEQ ID NO:347), Figure 204 (SEQ ID NO:352), Figure 206 (SEQ ID NO:354), Figure 208 (SEQ ID NO:356), Figure 168 (SEQ ID NO:302), Figure 170 (SEQ ID NO:304), Figure 172 (SEQ ID NO:306), Figure 174 (SEQ ID 154 (SEQ ID NO:273), Figure 156 (SEQ ID NO:275), Figure 158 (SEQ ID NO:277), Figure 160 (SEQ ID NO:265), Figure 148 (SEQ ID NO:267), Figure 150 (SEQ ID NO:269), Figure 152 (SEQ ID NO:271), Figure 140 (SEQ ID NO:248), Figure 142 (SEQ ID NO:253), Figure 144 (SEQ ID NO:250), Figure 146 (SEQ ID (SEQ ID NO:132), Figure 78 (SEQ ID NO:134), Figure 80 (SEQ ID NO:136), Figure 82 (SEQ ID NO:138), NO:118), Figure 70 (SEQ ID NO:123), Figure 72 (SEQ ID NO:128), Figure 74 (SEQ ID NO:130), Figure 76 (SEQ ID NO:77), Figure 48 (SEQ ID NO:79), Figure 50 (SEQ ID NO:84), Figure 52 (SEQ ID NO:86), Figure NO:52), Figure 32 (SEQ ID NO:54), Figure 34 (SEQ ID NO:56), Figure 36 (SEQ ID NO:58), Figure 38 (SEQ NO:429) and Figure 246 (SEQ ID NO:431). NO:372), Figure 218 (SEQ ID NO:374), Figure 220 (SEQ ID NO:376), Figure 222 (SEQ ID NO:378), Figure NO:328), Figure 190 (SEQ ID NO:330), Figure 192 (SEQ ID NO:332), Figure 194 (SEQ ID NO:334), Figure 182 (SEQ ID NO:322), Figure 184 (SEQ ID NO:324), Figure 186 (SEQ ID NO:326), Figure 188 (SEQ ID NO:212), Figure 120 (SEQ ID NO:214), Figure 122 (SEQ ID NO:216), Figure 124 (SEQ ID NO:218), Figure 112 (SEQ ID NO:198), Figure 114 (SEQ ID NO:203), Figure 116 (SEQ ID NO:210), Figure 118 (SEQ ID NO:180), Figure 106 (SEQ ID NO:189), Figure 108 (SEQ ID NO:194), Figure 110 (SEQ ID NO:196), Figure Figure 84 (SEQ ID NO:140), Figure 86 (SEQ ID NO:142), Figure 88 (SEQ ID NO:144), Figure 90 (SEQ ID Figure 62 (SEQ ID NO:104), Figure 64 (SEQ ID NO:111), Figure 66 (SEQ ID NO:116), Figure 68 (SEQ ID ID NO:63), Figure 40 (SEQ ID NO:68), Figure 42 (SEQ ID NO:70), Figure 44 (SEQ ID NO:72), Figure 46 Figure 24 (SEQ ID NO:41), Figure 26 (SEQ ID NO:43), Figure 28 (SEQ ID NO:50), Figure 30 (SEQ ID (SEQ ID NO:10), Figure 10 (SEQ ID NO:12), Figure 12 (SEQ ID NO:17), Figure 14 (SEQ ID NO:22), Figure sequence shown in Figure 2 (SEQ ID NO:4), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 8 encodes a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid An isolated nucleic acid having at least 80% sequence identity to a nucleotide sequence tha

5 207 (SEQ ID NO:355), Figure 209 (SEQ ID NO:357), Figure 211 (SEQ ID NO:363), Figure 213 (SEQ II NO:422), Figure 242 (SEQ ID NO:428) and Figure 245 (SEQ ID NO:430) 235 (SEQ ID NO:405), Figure 237 (SEQ ID NO:409), Figure 239 (SEQ ID NO:414), Figure 241 (SEQ ID NO:305), Figure 173 (SEQ ID NO:307). Figure 175 (SEQ ID NO:309), Figure 177 (SEQ ID NO:314), Figure NO:389), Figure 229 (SEQ ID NO:394), Figure 231 (SEQ ID NO:396), Figure 233 (SEQ ID NO:401), Figure 221 (SEQ ID NO:377), Figure 223 (SEQ ID NO:382), Figure 225 (SEQ ID NO:384), Figure 227 (SEQ ID NO:363), Figure 215 (SEQ ID NO:371), Figure 217 (SEQ ID NO:373), Figure 219 (SEQ ID NO:375), Figure NO:276), Figure 159 (SEQ ID NO:281), Figure 161 (SEQ ID NO:286), Figure 163 (SEQ ID NO:291), Figure NO:259), Figure 145 (SEQ ID NO:264), Figure 147 (SEQ ID NO:266), Figure 149 (SEQ ID NO:268), Figure 137 (SEQ ID NO:242), Figure 139 (SEQ ID NO:247), Figure 141 (SEQ ID NO:252), Figure 143 (SEQ ID (SEQ ID NO:115), Figure 67 (SEQ ID NO:117), Figure 69 (SEQ ID NO:122), Figure 71 (SEQ ID NO:127) NO:339), Figure 201 (SEQ ID NO:346), Figure 203 (SEQ ID NO:351), Figure 205 (SEQ ID NO:353), Figure 193 (SEQ ID NO:333), Figure 195 (SEQ ID NO:335), Figure 197 (SEQ ID NO:337), Figure 199 (SEQ ID NO:325), Figure 187 (SEQ ID NO:327), Figure 189 (SEQ ID NO:329), Figure 191 (SEQ ID NO:331), Figure 179 (SEQ ID NO:316), Figure 181 (SEQ ID NO:321), Figure 183 (SEQ ID NO:323), Figure 185 (SEQ ID NO:226). Figure 131 (SEQ ID NO:228), Figure 133 (SEQ ID NO:233), Figure 135 (SEQ ID NO:235), Figure NO:169), Figure 103 (SEQ ID NO:179), Figure 105 (SEQ ID NO:188), Figure 107 (SEQ ID NO:193), Figure ID NO:49), Figure 29 (SEQ ID NO:51), Figure 31 (SEQ ID NO:53), Figure 33 (SEQ ID NO:55), Figure 35 165 (SEQ ID NO:296), Figure 167 (SEQ ID NO:301), Figure 169 (SEQ ID NO:303), Figure 171 (SEQ ID 151 (SEQ ID NO:270), Figure 153 (SEQ ID NO:272), Figure 155 (SEQ ID NO:274), Figure 157 (SEQ ID 123 (SEQ ID NO:217), Figure 125 (SEQ ID NO:219), Figure 127 (SEQ ID NO:224), Figure 129 (SEQ ID NO:209), Figure 117 (SEQ ID NO:211), Figure 119 (SEQ ID NO:213), Figure 121 (SEQ ID NO:215), Figure 109 (SEQ ID NO:195), Figure 111 (SEQ ID NO:197), Figure 113 (SEQ ID NO:202), Figure 115 (SEQ ID Figure 95 (SEQ ID NO:157), Figure 97 (SEQ ID NO:159), Figure 99 (SEQ ID NO:161), Figure 101 (SEQ ID (SEQ ID NO:143), Figure 89 (SEQ ID NO:145), Figure 91 (SEQ ID NO:147), Figure 93 (SEQ ID NO:152) NO:133), Figure 81 (SEQ ID NO:137), Figure 83 (SEQ ID NO:139), Figure 85 (SEQ ID NO:141), Figure 87 Higure 73 (SEQ ID NO:129), Figure 75 (SEQ ID NO:131), Figure 77 (SEQ ID NO:133), Figure 79 (SEQ ID NO:99), Figure 59 (SEQ ID NO:101), Figure 61 (SEQ ID NO:103), Figure 63 (SEQ ID NO:110), Figure 65 Figure 51 (SEQ ID NO:85), Figure 53 (SEQ ID NO:87), Figure 53 (SEQ ID NO:94), Figure 57 (SEQ ID 43 (SEQ ID NO:71), Figure 45 (SEQ ID NO:76), Figure 47 (SEQ ID NO:78), Figure 49 (SEQ ID NO:83) (SEQ ID NO:57), Figure 37 (SEQ ID NO:62), Figure 39 (SEQ ID NO:67), Figure 41 (SEQ ID NO:69), Figure NO:30), Figure 21 (SEQ ID NO:32), Figure 23 (SEQ ID NO:40), Figure 25 (SEQ ID NO:42), Figure 27 (SEQ Figure 13 (SEQ ID NO:21), Figure 15 (SEQ ID NO:23), Figure 17 (SEQ ID NO:28), Figure 19 (SEQ ID Figure 5 (SEQ ID NO:7), Figure 7 (SEQ ID NO:9), Figure 9 (SEQ ID NO:11), Figure 11 (SEQ ID NO:16) se lected from the group consisting of the sequence shown in Figure 1 (SEQ ID NO:3), Figure 3 (SEQ ID NO:5) The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequenc

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ĸ છ 25 8 12 NO:414), Figure 241 (SEQ ID NO:422), Figure 242 (SEQ ID NO:428) and Figure 245 (SEQ ID NO:430) NO:303), Figure 171 (SEQ ID NO:305), Figure 173 (SEQ ID NO:307), Figure 175 (SEQ ID NO:309), Figure (SEQ 1D NO:42), Figure 27 (SEQ ID NO:49), Figure 29 (SEQ ID NO:51), Figure 31 (SEQ ID NO:53), Figure 233 (SEQ ID NO:401), Figure 235 (SEQ ID NO:405), Figure 237 (SEQ ID NO:409), Figure 239 (SEQ ID NO:384), Figure 227 (SEQ ID NO:389), Figure 229 (SEQ ID NO:394), Figure 231 (SEQ ID NO:396), Figure 219 (SEQ ID NO:375), Figure 221 (SEQ ID NO:377), Figure 223 (SEQ ID NO:382), Figure 225 (SEQ ID NO:363), Figure 213 (SEQ ID NO:365), Figure 215 (SEQ ID NO:371), Figure 217 (SEQ ID NO:373), Figure 205 (SEQ ID NO:353), Figure 207 (SEQ ID NO:355), Figure 209 (SEQ ID NO:357), Figure 211 (SEQ ID NO:323), Figure 185 (SEQ ID NO:325), Figure 187 (SEQ ID NO:327), Figure 189 (SEQ ID NO:329), Figure 177 (SEQ ID NO:314), Figure 179 (SEQ ID NO:316), Figure 181 (SEQ ID NO:321), Figure 183 (SEQ ID NO:274), Figure 157 (SEQ ID NO:276), Figure 159 (SEQ ID NO:281), Figure 161 (SEQ ID NO:286), Figure NO:252), Figure 143 (SEQ ID NO:259), Figure 145 (SEQ ID NO:264), Figure 147 (SEQ ID NO:266), Figure 135 (SEQ ID NO:235), Figure 137 (SEQ ID NO:242), Figure 139 (SEQ ID NO:247), Figure 141 (SEQ ID NO:161), Figure 101 (SEQ ID NO:169), Figure 103 (SEQ ID NO:179), Figure 105 (SEQ ID NO:188), Figure 63 (SEQ ID NO:110), Figure 65 (SEQ ID NO:115), Figure 67 (SEQ ID NO:117), Figure 69 (SEQ ID NO:122) NO:337), Figure 199 (SEQ ID NO:339), Figure 201 (SEQ ID NO:346), Figure 203 (SEQ ID NO:351), Figure 191 (SEQ ID NO:331), Figure 193 (SEQ ID NO:333), Figure 195 (SEQ ID NO:335), Figure 197 (SEQ ID 163 (SEQ ID NO:291), Figure 165 (SEQ ID NO:296), Figure 167 (SEQ ID NO:301), Figure 169 (SEQ ID 149 (SEQ ID NO:268), Figure 151 (SEQ ID NO:270), Figure 153 (SEQ ID NO:272), Figure 155 (SEQ ID NO:224), Figure 129 (SEQ ID NO:226), Figure 131 (SEQ ID NO:228), Figure 133 (SEQ ID NO:233), Figure 121 (SEQ ID NO:215), Figure 123 (SEQ ID NO:217), Figure 125 (SEQ ID NO:219), Figure 127 (SEQ ID NO:202), Figure 115 (SEQ ID NO:209), Figure 117 (SEQ ID NO:211), Figure 119 (SEQ ID NO:213), Figure 107 (SEQ ID NO:193), Figure 109 (SEQ ID NO:195), Figure 111 (SEQ ID NO:197), Figure 113 (SEQ ID (SEQ ID NO:141), Figure 87 (SEQ ID NO:143), Figure 89 (SEQ ID NO:145), Figure 91 (SEQ ID NO:147), NO:133), Figure 79 (SEQ ID NO:135), Figure 81 (SEQ ID NO:137), Figure 83 (SEQ ID NO:139), Figure 85 Figure 71 (SEQ ID NO:127), Figure 73 (SEQ ID NO:129), Figure 75 (SEQ ID NO:131), Figure 77 (SEQ ID Figure 93 (SEQ ID NO:152), Figure 95 (SEQ ID NO:157), Figure 97 (SEQ ID NO:159), Figure 99 (SEQ ID ID NO:94), Figure 57 (SEQ ID NO:99), Figure 59 (SEQ ID NO:101), Figure 61 (SEQ ID NO:103), Figure NO:78), Figure 49 (SEQ ID NO:83), Figure 51 (SEQ ID NO:85), Figure 53 (SEQ ID NO:87), Figure 55 (SEQ Figure 41 (SEQ ID NO:69), Figure 43 (SEQ ID NO:71), Figure 45 (SEQ ID NO:76), Figure 47 (SEQ ID 33 (SEQ ID NO:55), Figure 35 (SEQ ID NO:57), Figure 37 (SEQ ID NO:62), Figure 39 (SEQ ID NO:67), NO:11), Figure 11 (SEQ ID NO:16), Figure 13 (SEQ ID NO:21), Figure 15 (SEQ ID NO:23), Figure 17 (SEQ ID NO:3), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 7 (SEQ ID NO:9), Figure 9 (SEQ ID ID NO:28), Figure 19 (SEQ:ID NO:30), Figure 21 (SEQ ID NO:32), Figure 23 (SEQ ID NO:40), Figure 25 selected from the group consisting of the full-length coding sequence of the sequence shown in Figure 1 (SEQ The nucleic acid of Claim 1, wherein said nucleoride sequence comprises a nucleotide sequence

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 Isolated nucleic acid which comprises the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 2.

- A vector comprising the nucleic acid of Claim 1.
- The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.
- A host cell comprising the vector of Claim 5

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The bost cell of Claim 7 wherein said cell is a CHO cell

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- The host cell of Claim 7 wherein said cell is an E. coll.
- The bost cell of Claim 7 wherein said cell is a yeast cell

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- 11. A process for producing a PRO polypeptides comprising culturing the host cell of Chim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.
- ራ 30 ĸ 20 102 (SEQ ID NO:170), Figure 104 (SEQ ID NO:180), Figure 106 (SEQ ID NO:189), Figure 108 (SEQ ID Figure 66 (SEQ ID NO:116), Figure 68 (SEQ ID NO:118), Figure 70 (SEQ ID NO:123), Figure 72 (SEQ ID 28 (SEQ ID NO:50), Figure 30 (SEQ ID NO:52), Figure 32 (SEQ ID NO:54), Figure 34 (SEQ ID NO:56) 116 (SEQ ID NO:210), Figure 118 (SEQ ID NO:212), Figure 120 (SEQ ID NO:214), Figure 122 (SEQ ID (SEQ ID NO:136), Figure 82 (SEQ ID NO:138), Figure 84 (SEQ ID NO:140), Figure 86 (SEQ ID NO:142) NO:128), Figure 74 (SEQ ID NO:130), Figure 76 (SEQ ID NO:132), Figure 78 (SEQ ID NO:134), Figure 80 ID NO:84), Figure 52 (SEQ ID NO:85), Figure 54 (SEQ ID NO:85), Figure 56 (SEQ ID NO:95), Figure 58 Figure 36 (SEQ ID NO:58), Figure 38 (SEQ ID NO:63), Figure 40 (SEQ ID NO:68), Figure 42 (SEQ ID ID NO:17), Figure 14 (SEQ ID NO:22), Figure 16 (SEQ ID NO:24), Figure 18 (SEQ ID NO:29), Figure 20 ID NO:6), Figure 6 (SEQ ID NO:8), Figure 8 (SEQ ID NO:10), Figure 10 (SEQ ID NO:12), Figure 12 (SEQ NO:153), Figure 96 (SEQ ID NO:158), Figure 98 (SEQ ID NO:160), Figure 100 (SEQ ID NO:162), Figure Figure 88 (SEQ ID NO:144), Figure 90 (SEQ ID NO:146), Figure 92 (SEQ ID NO:148), Figure 94 (SEQ ID (SEQ ID NO:100), Figure 60 (SEQ ID NO:102), Figure 62 (SEQ ID NO:104), Figure 64 (SEQ ID NO:111) NO:70), Figure 44 (SEQ ID NO:72), Figure 46 (SEQ ID NO:77), Figure 48 (SEQ ID NO:79), Figure 50 (SEQ (SEQ ID NO:31), Figure 22 (SEQ ID NO:33), Figure 24 (SEQ ID NO:41), Figure 26 (SEQ ID NO:43), Figure NO:194), Figure 110 (SEQ ID NO:196), Figure 112 (SEQ ID NO:198), Figure 114 (SEQ ID NO:203), Figure sclected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:4), Figure 4 (SEQ Isolated PRO polypeptide having at least 80% sequence identity to an amino acid sequence

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2 NO:332), Figure 194 (SEQ ID NO:334), Figure 196 (SEQ ID NO:336), Figure 198 (SEQ ID NO:338), Figure 158 (SEQ ID NO:277), Figure 160 (SEQ ID NO:282), Figure 162 (SEQ ID NO:287), Figure 164 (SEQ ID 228 (SEQ ID NO:390), Figure 230 (SEQ ID NO:395), Figure 232 (SEQ ID NO:397), Figure 234 (SEQ ID NO:376), Figure 222 (SEQ ID NO:378), Figure 224 (SEQ ID NO:383), Figure 226 (SEQ ID NO:385), Figure NO:402), Figure 236 (SEQ ID NO:406), Figure 238 (SEQ ID NO:410), Figure 240 (SEQ ID NO:415), Figure 214 (SEQ ID NO:366), Figure 216 (SEQ ID NO:372), Figure 218 (SEQ ID NO:374), Figure 220 (SEQ ID NO:354), Figure 208 (SEQ ID NO:356), Figure 210 (SEQ ID NO:358), Figure 212 (SEQ ID NO:364), Figure 200 (SEQ ID NO:340), Figure 202 (SEQ ID NO:347), Figure 204 (SEQ ID NO:352), Figure 206 (SEQ ID 186 (SEQ ID NO:326), Figure 188 (SEQ ID NO:328), Figure 190 (SEQ ID NO:330), Figure 192 (SEQ ID NO:315), Figure 180 (SEQ ID NO:317), Figure 182 (SEQ ID NO:322), Figure 184 (SEQ ID NO:324), Figure 172 (SEQ ID NO:306), Figure 174 (SEQ ID NO:308), Figure 176 (SEQ ID NO:310), Figure 178 (SEQ ID NO.292), Figure 166 (SEQ ID NO:297), Figure 168 (SEQ ID NO:302), Figure 170 (SEQ ID NO:304), Figure NO:269), Figure 152 (SEQ ID NO:271), Figure 154 (SEQ ID NO:273), Figure 156 (SEQ ID NO:275), Figure 144 (SEQ ID NO:260), Figure 146 (SEQ ID NO:265), Figure 148 (SEQ ID NO:267), Figure 159 (SEQ ID NO:236), Figure 138 (SEQID NO:243), Figure 140 (SEQID NO:248), Figure 142 (SEQID NO:253), Figure 130 (SEQ ID NO:227), Figure i32 (SEQ ID NO:229), Figure 134 (SEQ ID NO:234), Figure 136 (SEQ ID NO:216), Figure 124 (SEQ ID NO:218), Figure 126 (SEQ ID NO:220), Figure 128 (SEQ ID NO:225), Figure

Isolaird PRO polypeptide having at least 80% sequence identity to the amino acid sequence
 cnooded by a methic acid molecule deposited under my ATCC accession number shown in Table 2.

242 (SEQ ID NO:423), Figure 244 (SEQ ID NO:429) and Figure 246 (SEQ ID NO:431).

- A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.
- 25 15. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is an epitope tag acquemee.
- 16. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is a Fe region of an immunoglobulin.
- An antibody which specifically binds to a PRO polypepside according to Claim 12.

- The antibody of Claim 17 wherein said antibody is a monoclonal antibody
- The unibody of Claim 17 wherein said antibody is a humanized antibody
- The antibody of Claim 17 wherein said antibody is an antibody fragment.

₽ Figure 242 (SEQ ID NO:428) and Figure 245 (SEQ ID NO:430) ID NO:335), Figure 209 (SEQ ID NO:357), Figure 211 (SEQ ID NO:363), Figure 213 (SEQ ID NO:365) Figure 173 (SEQ ID NO:307), Figure 175 (SEQ ID NO:309), Figure 177 (SEQ ID NO:314), Figure 179 (SEC ID NO:405), Figure 237 (SEQ ID NO:409), Figure 239 (SEQ ID NO:414), Figure 241 (SEQ ID NO:422) ID NO:333), Figure 195 (SEQ ID NO:335), Figure 197 (SEQ ID NO:337), Figure 199 (SEQ ID NO:339) ID NO:316), Figure 181 (SEQ ID NO:321), Figure 183 (SEQ ID NO:323), Figure 185 (SEQ ID NO:325) ID NO:270), Figure 153 (SEQ ID NO:272), Figure 155 (SEQ ID NO:274), Figure 157 (SEQ ID NO:276) ID NO:242), Figure 139 (SEQ ID NO:247), Figure 141 (SEQ ID NO:252), Figure 143 (SEQ ID NO:259) Figure 103 (SEQ ID NO:179), Figure 105 (SEQ ID NO:188), Figure 107 (SEQ ID NO:193), Figure 109 (SEQ NO:115), Figure 67 (SEQ ID NO:117), Figure 69 (SEQ ID NO:122), Figure 71 (SEQ ID NO:127), Figure 73 Figure 229 (SEQ ID NO:394), Figure 231 (SEQ ID NO:396), Figure 233 (SEQ ID NO:401), Figure 235 (SEQ ID NO:377), Figure 223 (SEQ ID NO:382), Figure 225 (SEQ ID NO:384), Figure 227 (SEQ ID NO:389) Figure 215 (SEQ ID NO:371), Figure 217 (SEQ ID NO:373), Figure 219 (SEQ ID NO:375), Figure 221 (SEQ Figure 201 (SEQ ID NO:346), Figure 203 (SEQ ID NO:351), Figure 205 (SEQ ID NO:353), Figure 207 (SEQ Figure 187 (SEQ ID NO:327), Figure 189 (SEQ ID NO:329), Figure 191 (SEQ ID NO:331), Figure 193 (SEQ ID NO:296), Figure 167 (SEQ ID NO:301), Figure 169 (SEQ ID NO:303), Figure 171 (SEQ ID NO:305) Figure 159 (SEQ ID NO:281), Figure (61 (SEQ ID NO:286), Figure 163 (SEQ ID NO:291), Figure 165 (SEC Figure 145 (SEQ ID NO:264), Figure 147 (SEQ ID NO:266), Figure 149 (SEQ ID NO:268), Figure 151 (SEQ Figure 131 (SEQ ID NO:228), Figure 133 (SEQ ID NO:233), Figure 135 (SEQ ID NO:235), Figure 137 (SEQ ID NO:217), Figure 125 (SEQ ID NO:219), Figure 127 (SEQ ID NO:224), Figure 129 (SEQ ID NO:226) Figure 117 (SEQ ID NO:211), Figure 119 (SEQ ID NO:213), Figure 121 (SEQ ID NO:215), Figure 123 (SEQ ID NO:195), Figure 111 (SEQ ID NO:197), Figure 113 (SEQ ID NO:202), Figure 115 (SEQ ID NO:209), Figure 81 (SEQ ID NO:137), Figure 83 (SEQ ID NO:139), Figure 85 (SEQ ID NO:141), Figure 87 (SEQ ID 51 (SEQ ID NO:85), Figure 53 (SEQ ID NO:87), Figure 55 (SEQ ID NO:94), Figure 57 (SEQ ID NO:99) ID NO:57), Figure 37 (SEQ ID NO:62), Figure 39 (SEQ ID NO:67), Figure 41 (SEQ ID NO:69), Figure 43 NO:49), Figure 29 (SEQ ID NO:51), Figure 31 (SEQ ID NO:53), Figure 33 (SEQ ID NO:55), Figure 35 (SEQ Figure 21 (SEQ ID NO:32), Figure 23 (SEQ ID NO:40), Figure 25 (SEQ ID NO:42), Figure 27 (SEQ ID (SEQ ID NO:157), Figure 97 (SEQ ID NO:159), Figure 99 (SEQ ID NO:161), Figure 101 (SEQ ID NO:169), NO:143), Figure 89 (SEQ ID NO:145), Figure 91 (SEQ ID NO:147), Figure 93 (SEQ ID NO:152), Figure 95 (SEQ ID NO:129), Figure 75 (SEQ ID NO:131), Figure 77 (SEQ ID NO:133), Figure 79 (SEQ ID NO:135) (SEQ ID NO:71), Figure 45 (SEQ ID NO:76), Figure 47 (SEQ ID NO:78), Figure 49 (SEQ ID NO:83). Figure Figure 59 (SEQ ID NO:101), Figure 61 (SEQ ID NO:103), Figure 63 (SEQ ID NO:110), Figure 65 (SEQ ID 13 (SEQ ID NO:21), Figure 15 (SEQ ID NO:23), Figure 17 (SEQ ID NO:28), Figure 19 (SEQ ID NO:30) 5 (SEQ ID NO:7), Figure 7 (SEQ ID NO:9), Figure 9 (SEQ ID NO:11), Figure 11 (SEQ ID NO:16), Figure selected from the group consisting of that shown in Figure 1 (SEQ ID NO:3), Figure 3 (SEQ ID NO:5), Figure An isolated nucleic acid which has at least 80% sequence identity to a nucleic acid sequence

> WO 00/12708 PCT/US99/20111

35 30 25 20 5 5 NO:161), Figure 101 (SEQ ID NO:169), Figure 103 (SEQ ID NO:179), Figure 105 (SEQ ID NO:188), Figure (SEQ ID NO:110), Figure 65 (SEQ ID NO:115), Figure 67 (SEQ ID NO:117), Figure 69 (SEQ ID NO:122), 135 (SEQ ID NO:235), Figure 137 (SEQ ID NO:242), Figure 139 (SEQ ID NO:247), Figure 141 (SEQ ID ID NO:42), Figure 27 (SEQ ID NO:49), Figure 29 (SEQ ID NO:51), Figure 31 (SEQ ID NO:53), Figure 33 NO:414), Figure 241 (SEQ ID NO:422), Figure 242 (SEQ ID NO:428) and Figure 245 (SEQ ID NO:430) NO:384), Figure 227 (SEQ ID NO:389), Figure 229 (SEQ ID NO:394), Figure 231 (SEQ ID NO:396), Figure 219 (SEQ ID NO:375), Figure 221 (SEQ ID NO:377), Figure 223 (SEQ ID NO:382), Figure 225 (SEQ ID NO:363), Figure 213 (SEQ ID NO:365), Figure 215 (SEQ ID NO:371), Figure 217 (SEQ ID NO:373), Figure 205 (SEQ ID NO:353), Figure 207 (SEQ ID NO:355), Figure 209 (SEQ ID NO:357), Figure 211 (SEQ ID NO:337), Figure 199 (SEQ ID NO:339), Figure 201 (SEQ ID NO:346), Figure 203 (SEQ ID NO:351), Figure NO:303), Figure 171 (SEQ ID NO:305), Figure 173 (SEQ ID NO:307), Figure 175 (SEQ ID NO:309), Figure 149 (SEQ ID NO:268), Figure 151 (SEQ ID NO:270), Figure 153 (SEQ ID NO:272), Figure 155 (SEQ ID NO:202), Figure 115 (SEQ ID NO:209), Figure 117 (SEQ ID NO:211), Figure 119 (SEQ ID NO:213), Figure NO:94), Figure 57 (SEQ ID NO:99), Figure 59 (SEQ ID NO:101), Figure 61 (SEQ ID NO:103), Figure 63 233 (SEQ ID NO:401), Figure 235 (SEQ ID NO:405), Figure 237 (SEQ ID NO:409), Figure 239 (SEQ ID 191 (SEQ ID NO:331), Figure 193 (SEQ ID NO:333), Figure 195 (SEQ ID NO:335), Figure 197 (SEQ ID NO:323), Figure 185 (SEQ ID NO:325), Figure 187 (SEQ ID NO:327), Figure 189 (SEQ ID NO:329), Figure 177 (SEQ ID NO:314), Figure 179 (SEQ ID NO:316), Figure 181 (SEQ ID NO:321), Figure 183 (SEQ ID 163 (SEQ ID NO:291), Figure 165 (SEQ ID NO:296), Figure 167 (SEQ ID NO:301), Figure 169 (SEQ ID NO:274), Figure 157 (SEQ ID NO:276), Figure 159 (SEQ ID NO:281), Figure 161 (SEQ ID NO:286), Figure NO:252), Figure 143 (SEQ ID NO:259), Figure 145 (SEQ ID NO:264), Figure 147 (SEQ ID NO:266), Figure NO:224), Figure 129 (SEQ ID NO:226), Figure 131 (SEQ ID NO:228), Figure 133 (SEQ ID NO:233), Figure 121 (SEQ ID NO:215), Figure 123 (SEQ ID NO:217), Figure 125 (SEQ ID NO:219), Figure 127 (SEQ ID 107 (SEQ ID NO:193), Figure 109 (SEQ ID NO:195), Figure 111 (SEQ ID NO:197), Figure 113 (SEQ ID Figure 93 (SEQ ID NO:152), Figure 95 (SEQ ID NO:157), Figure 97 (SEQ ID NO:159), Figure 99 (SEQ ID (SEQ ID NO:141), Figure 87 (SEQ ID NO:143), Figure 89 (SEQ ID NO:145), Figure 91 (SEQ ID NO:147), NO:133), Figure 79 (SEQ ID NO:135), Figure 81 (SEQ ID NO:137), Figure 83 (SEQ ID NO:139), Figure 85 Figure 71 (SEQ ID NO:127), Figure 73 (SEQ ID NO:129), Figure 75 (SEQ ID NO:131), Figure 77 (SEQ ID Figure 49 (SEQ ID NO:83), Figure 51 (SEQ ID NO:85), Figure 53 (SEQ ID NO:87), Figure 55 (SEQ ID 41 (SEQ ID NO:69), Figure 43 (SEQ ID NO:71), Figure 45 (SEQ ID NO:76), Figure 47 (SEQ ID NO:78) (SEQ ID NO:55), Figure 35 (SEQ ID NO:57), Figure 37 (SEQ ID NO:62), Figure 39 (SEQ ID NO:67), Figure NO:28), Figure 19 (SEQ ID NO:30), Figure 21 (SEQ ID NO:32), Figure 23 (SEQ ID NO:40), Figure 25 (SEQ Figure 11 (SEQ ID NO:16), Figure 13 (SEQ ID NO:21), Figure 15 (SEQ ID NO:23), Figure 17 (SEQ ID Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 7 (SEQ ID NO:9), Figure 9 (SEQ ID NO:11) sequence of a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:3) An isolated nucleic acid which has at least 80% sequence identity to the full-length codin

23. An isolated extracellular domain of a PRO polypeptide ž

೪

25

20

- An isolated PRO polypeptide lacking its associated signal peptide
- 25. An isolated polypeptide having at least about 80% amino acid sequence identity to an extracellular domain of of PRO polypeptide.
- 26. An isolated polypeptide having at least about 80% amino acid sequence identity to a PRO polypeptide lacking its associated signal peptide.
- An isolated nucleic acid encoding the polypeptide of any one of Claims 23 to 26.

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FIGURE 1

TCAATCAAGATGTATGTTTGCTATGTTCTAAGTCCACCTTCTATCCCATTCATGTTAGATCG GTAGACCTAAAACTACACCAATAGGCTGATTCAATCAAGATCCGTGCTCGCAGTGGGCTGAT CTACCTTTAAGGACATTTAGGGTCCCCCCCTGTGAATTAGAAAGTTGCTTGGCTGGAGAACTG ATTTCCTTTGGAGTTGCTTGCTTCCAACTGATTGGAATCTTTCTCGCCTACTGCCWCTCTCG ATGAAGGTTGTTTTATAAAGGTGATGACCATTATAGAGTCAGAAATGGGAGTCGTTGCAGGA TCCTAAGAGTTGCTGTAAACTTGAAGATTGTACTCCACAGAGAGATGCAGACAAAGTAAACA TGTTGTGGTGTCACCGATTATAGAGATTGGACAGATACTAATTATTACTCAGAAAAAGGATT ATTTGTTTTCAGACATGAGATTAAGAACAGCTTTAAGAATAATTATGAGAAGGCTTTGAAGC AAACTGTATGCAATGTTTCTGACTCTCGTTTTTTTGGTCGAACTGGTCGCTGCCATCGTAGG TCATTATTCTTTTGGGCACCTTTGGTTGTTTTTGCTACCTGCCGAGCTTCTGCATGGATGCTA CTTTTCTCTTTTAAATGAGAAGGCCACCAATGTCCCCCTTCGTGCTCATTGCTACTGGTACCG TGGATCACTGGCGTTATCCTTCTTGCAGTTGGCATTTGGGGCCAAGGTGAGCCTGGAGAATTA TGCAGACTAAACCAGICATTACTTGTTTCAAGAGCGTTCTGCTAATCTACACTTTTATTTTC CCAATCGCCCGGTGCGGTGCAGGGTTTCGGGCTAGTCATGGCGTCCCCGTCTCGGAGAC TTGAAACCCTGTATCCCTCTGAAACACTGGAAGAGCTAGTAAATTGTAAATGAAGT TGCCATAACAAATAACCAGTATGAGATAGTG<u>TAA</u>CCCAATGTATCTGTGGGCCTATTCCTCT AGTATAACTCTACAGGAGATTATAGAAGCCATGCAGTAGACAAGATCCAAAATACGTTGCAT

FIGURE 2

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA19902
><subunit 1 of 1, 245 aa, 1 stop, 1 unknown
><subunit 1 of 1, 245 aa, 1 stop, 1 unknown
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VLIATGTVIILLGTFGCFATCRASAMMLKT,YAMFLTLVFLVELVAAIVGFVFRHEIKNSFKN
NYEKALKQXNSTGDYRSHAVDKIQNTLHCCGVTDYRDWTDTNYYSEKGFPKSCCKLEDCTPQ
RDADKVNNEGCFIKVMTIIESEMGVVAGISFGVACFQLIGIFLAYCXSRAITUNQYEIV</pre>

Important features of the protein: Signal peptide:

amino acids 1-42

Transmambrane domains: amino acids 19-42, 61-83, 92-114, 209-230,

N-glycosylation site. amino acids 134-138

Tyrosine kinase phosphorylation site. amino acids 160-168, 160-169

N-myristoylation site.
amino acids 75-81, 78-84, 210-216, 214-220, 226-232

Prokaryotic membrane lipoprotein lipid attachment site. amino acids 69-80, 211-222

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FIGURE 3

TGATAAGATTTGATGTTTTTGCTTGCTGTCATCTACTTTGTCTGGAAATGTCTAAATGTTTC CCAAGCCTTGTGCTCACAGGGCAAAGGAGAATATTTTAATGCTCCGCTGATGGCAGAGTAAA GAAAAGTGTTCTGCCCGGAACCATGACTTTAGGACTCCTTCAGTTCCTTTAGGACATACTCG GGCAGTAATACGGACTCTTGTAGATAAG<u>TAA</u>GTATCTGACTCACGGTCACCTCCAGTGGAAT CGAGGACCTCATGAGCCAAGGAGAAAAGAAACAAAATGTGGATGGGCTAGTGTTGGACACACT CAGTACCCACTGCTGACACAAGGAGCCAACCACGGGACCCTGTTCGGCCGACCAAGGAGGGGGC CCGAGATGACAGTGGAACAGATGACAGTGTTGACACCCGAACAGCAACAGGCCGAGAACAGTG CACATAGCCCACTTCCTAGGGACTGGAGGTGCCGCTACTACCATGGGTAATTCCTGTATCTG GTTGGGCCGTGTTCTTAGCGAGCAGAAGCCTTGGCCAGGGTCTGTTGTTGACTCTCGAAGAG GGAATAAGCTCTGCAACTTTCTTTGGCATTCNGTTGTTAAAAACAAATAGGATGCAAATTCC GCGGCTAACAGGGCCCAGAACTGCCATTGGATGTCCAGAATCCCCTGTAGTTGATAATGTTG GTTCCCTCTTTCGGGGGTCCTCACCAGAAGAGGTTCTTGGGGGTCGCCCTTCTGAGGAGGCT GCCGAGAGGTTTTCCACCGAGGCCCGCGCTTGAGGGATCTGAAGAGGGTTCCTAGAAGAGGGT GCCGGGGTAGGCTCTGGAAAGGGCCCGGGAGAGAGGTGGCGTTGGTCAGAACCTGAGAAACA GAAGTCGCGCCGCCGCCCCCCCCCCCCCCCGGGGCCCCGGGAGGTAGAGAAAAGTCAGT CCCACGCGTCCGGCGCCGTGGCCTCGCGTCCATCTTTGCCGTTCTCTCGGACCTGTCACAAA TGTAGCAGAAAACACGATAAAGCTATGATCTTTATTAGAG TCAACTCCAGGTTATGAAAACAGTACTTGGAAAACTGAAAACTACCTAA<u>ATG</u>ATCGTCTTTG

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FIGURE 4

AENSAVPTADTRSQPRDPVRPPRRGRGPHEPRRKKQNVDGLVLDTLAVIRTLVDKO MIVFGWAVFLASRSLGQGLLLTLEEHIAHFLGTGGAATTMGNSCICRDDSGTDDSVDTQQQQ

Signal peptide:

amino acids 1-16

amino acids 22-26, 50-54, 113-117 Casein kinase II phosphorylation site.

amino acids 18-24, 32-38, 34-40, 35-41, 51-57 N-myristoylation site.

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FIGURE 5

TCTCTTTGCAATCTGGGCTGCGTCCTGAGCAATGGGCTCTGTCTCGCTGGCCCTTGCCCTGGA GAGAGAACGACCCCAAGTACAGTGCTCTCCGCCAGAATTTCTTCCGCTACCATGGGCTGTCC GCGAGGCCTGGGTGGGGAGGTACCAGGCAGCCACCAGGGTCCCGATCCCTACCGCCAGCTGC GCCCGCTGGCTGGAACCCCCGCACCACAGCTGCCATGTGGGCCCTGCAAACCGTGGAGAAGGA CATTCTGGGAGGCCAGCCAGCTTTACCTGCTGTTCCTGAGCCTTACGCTGGCCACTGTCAAC CATGGGCTGTGCCTTCATCAACCTCTGCATCTTGGCTTCACAGCATGCTTGGGCTCAGCTCA CTTCCCCGACATACCTTCGGACTAGTGCAGAGCAAACTCTTCCCCCTTCTACTTCCACATCTC CAGGTGCCTGGGGCATGCAAATGTGGGTGACCTTCGTCTCAGGCTTCCTGCTTTTCCGAAGC CAAGATGGAGGAAGGCGGGAACCCCTGATTAAGATGGTCCATCTACTGGTCTTGT CCGACGCCTCTCTTCTCGGAATCCGGGTGCTGCGGATTGAGGTCCCGGTTCCTAACGGACTG GGCACGAGGCGCTGTCCACCCGGGGGGCGTGGGAGTGAGGTACCAGATTCAGCCCATTTGGCC AAAAAAAAAAA

IGURE 6

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56107

<subunit 1 of 1, 231 aa, 1 stop</pre>

<NX(S/T): 0

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Signal peptide:

amino acids 1-24

Transmembrane domain:

amino acids 86-103, 60-75

Casein kinase II phosphorylation site. amino acids 82-86

Tyrosine kinase phosphorylation site.

amino acids 144-151

N-myristoylation site.

amino acids 4-10, 5-11, 47-53, 170-176, 176-182

Prokaryotic membrane lipoprotein lipid attachment site.

amino acide 54-65

G-protein coupled receptors proteins.

amino acids 44-85

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FIGURE 7

TCCCAAGGCAGTG<u>TGA</u>CTCAGCTAACCACAAATGTCTCCTCCAGGCTATGAAATTGGCCGAT GACATCAAACAACAATATGGAGAAGGTTACATTGAAAAAAGTCTAGACAAACTGAAAGGCAA ATCGTTGGAGGGGGCTATACTCCATCCAAATATGCAGTGGAAGGTTTCAATGACAGCTTAAG CTACAGAGAACCTATTGAAGTGAACCTGTTTGGACTCATCAGTGTGACACTAAATATGCTTC AGAATGTCAAGAGGACTGCCCAGTGGGTGAAGAACCAAGTTGGGGAGAAAGGTCTCTGGGGT ACATCACTGATAAGTACATTTTTATCACTGGATGTGACTCGGGCTTTGGAAACTTGGCAGCC GCTAGGCCTCCTAATCCTCTGTGGTTTTCTGTGGACTCGTAAAGGAAAACTAAAGATTGAAG AATTCAGATTTTAAGCCCATTCTGCAGTGGAATTTCATGAACTAGCAAGAGGACACCATCTT aaraaaaaaaaaaaaaaa ATCTTTACCGTGGCCTGCCCCATGCTTATGGTCCCCAGCATTTACAGTAACTTGTGAATGTT ATTTAGGCTTTGCCTTGGTGTGATGTAAGGGAAATTGAAAGACTTGCCCATTCAAAATG CTCAAGTTTTCTTTGAAAAGGAGGGCTGGAATGGTACATCACATAGGCAAGTCCTGCCCTGT TCGTGCTTATTTGGATTGCAAAAGGGAGTCCCACCATCGCTGGTGGTATCCCAGGGTCCCTG TTCAAGAACACATCTCCTTTTCAACCCCATTCCTTATCTGCTCCAACCTGGACTCATTTAGA TCTCACATGCCAGCAGCTTTGCAAGACTTTTTATTGTTGAAACAGAAAGCAGAGCTGGCTAA GTCTCTTCCCTAAGACTCATTATGCCGCTGGAAAAAGATGCCAAAATTTTCTGGATACCTCTG TAAATCCTATGTGAACATGGACCTCTCTCCGGTGGTAGAGTGCATGGACCACGCTCTAACAA ACTTGGCAGATCCAGTAAAGGTAATTGAAAAAAAAACTCGCCATTTGGGAGCAGCTGTCTCCA ACGGGACATGAAAGCTTTTGGTGTGCACGTCTCATGCATTGAACCAGGATTGTTCAAAACAA CTTTGGTCAAGAAAGCTCAAGGGAGAGTTATTAATGTCTCCAGTGTTGGAGGTCGCCTTGCA CTTGTATTATACAAGAAAGGAGTGTACCTATCACACAGAGGGGGAAAA<u>ATG</u>CTCTTTTGGGT

FIGURE 8

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><subunit 1 of 1, 319 aa, 1 stop</pre>

><MW: 35227, pI: 8.97, NX(S/T): 3

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ESGSTALKAETSERLRTVLLDVTDPENVKRTAQWVKNQVGEKGLWGLINNAGVPGVLAPTDW
LTLEDYREPIEVNLFGLISVTLMMLPLVKKAQGRVINVSSVGGRLAIVGGGYTPSKYAVEGF
NDSLRRDMKAFGVHVSCIEPGLFKTNLADPVKVIEKKLAIWEQLSPDIKQQYGEGYIEKSLD
KLKGNKSYVNMDLSPVVECMDHALTSLFPKTHYAAGKDAKIFWIPLSHMPAALQDFLLLKQK
AELANPKAV

Important features of the protein:

Signal peptide:

amino acids 1-17

N-glycosylation sites.

Transmembrane domain: amino acids 136-152

amino acids 161-163, 187-190 and 253-256

Glycosaminoglycan attachment site.

amino acids 39-42

N-myristoylation sites.

amino acids 36-41, 42-47, 108-113, 166-171, 198-203 and 207-212

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EIGURE 9

CGCCACGGTGGACCTCCGACAGCACTGTGGCCGAGGTGACCAGCATTCAGCTGGAGTTCCGGGAGTTCCGGGAGCTCTCCCGTCTCACAGGGGGATAAGAAGTTTCAGGAGGGCAGTGGAGAAGGAGACACAGCACAGTGCACGGGCCTGTCTGGGAAGAAGGATGGGCTGGTGCCCATGTTCATCAATACCCACAGTG CTGAACTGGCTCTGGGCTCCTCGTCTCTGCTTTAATCAGGACACCGTGAGGACAAGTGA CTTCAGAACACCATCCAAGATTCCTTACTCGGATGTGAACATCGGTACTGGAGTTGCCCACC CCAGTGGAATGGGTCTTTTCGGTGGAGATAAAAGTTGATTTGCTCTAACCGCAA CTGGCCGCCGCAGGGGCTTGGAGGGCTGGACGGCAAGTCCGTCTAGCTCACGGGCCCCT CTCCAGAGGCCTGAGGCTCCAGGGCTGGCTCTGGTGTTTACAAGCTGGACTCAGGGATCCTC TCTGCCCGGGCTCGTGAAGCCTCAGATGTCCCCAATCCAAGGGTCTGGAGGGGCTGCCGTGA GAGGGGGGCTTCCAGGTGGTCCCTGGTACTGGGGTGACCGAGTGGACAGCCCAGGGTGCAGC CAGAAGACACGAATCATGACTCACGATTGCTGAAGCCTGAGCAGGTCTCTGTGGGCCGACCA GCCGTCAGTCTTGGTGTGATGCGGGGTGGGCTGGGCCGGTGGAGCCTCCGCCTGCTTCCTC CTGGGTCTGTGGCATTTTCCAAGGGCCCACGTAGCACCGGCAACCGCCAAGTGGCCCAGGCT GGACCCCTGCC<u>TAG</u>GGTGGATGGCTGCTGGTGTGGGGACTTCGGGTGGGCAGAGGCACCTTG CCCAAACCTGCTCAGCCTGGACGCCTACGTGTTCAACACCGAAGCCCACCCTCTGCCTATCT AAGATGGAGAGCTTCTTCCTGGGGGAGACGCTCAAGTATCTGTTCTTGCTCTTCTCCGATGA CCTCGGGTGGCTATTCTTCCATCAACAATGTCCAGGATCCTCAGAAGCCCGAGCCTAGGGAC CCGCAAATACCAGGACTGGGGGCTGGGAGATTCTGCAGAGCTTCAGCCGATTCACACGGGTCC CACAACCTGCTGCGGCCAGAGACCGTGGAGAGCCTGTTCTACCTGTACCGCGTCACAGGGGA TGCACTTCAACCTTTACCCCCAGCCGGGCCGTCGGGACGTGGAGGTCAAGCCAGCAGACAGG GCTCATGGAGACTTGTTACCAGATGAACCGGCAGATGGAGACGGGGGCTGAGTCCCGAGATCG TGGGGGAGCTTGCCCACGGCCGCTTCAGTGCCAAGATGGACCACCTGGTGTGCTTCCTGCCA AGCCATCGAGGGTGTCAGAACGCACCTGCTGCGGCACTCCGAGCCCAGTAAGCTCACCTTTG CTGCTGAAGCAGTGGATCCAGGGCGGGAAGCAGGAGACACAGCTGCTGGAAGACTACGTGGA GCCTCTTCACCCACCTGGGCGTATTCACGCTGGGCGCCAGGGCCGACAGCTACTATGAGTAC CTGTCTGGGGACAGCCTCTTCCTGAGGAAAGCTGAGGATTTTGGAAATCGGCTAATGCCTGC GAGGAAAGAATTTGAGGAAGCCAGGAAGTGGGTGTCGAAGAAGTTACACTTTGAAAAGGACG GAGTGGTTTGGCCTCGGTCTCACACTGATCGACGCGCTGGACACCATGTGGATCTTGGGTCT AAGGATACCGCAAGTTTGCATGGGGCCATGACGAGCTGAAGCCTGTGTCCAGGTÇCTTCAGT CTCCCTTCAAGAAGAGCAGAAGTGCCCACCAAGCCTCCCCTGCCACCGGCCAGGACACAGGG ATCCGCAGAGGACAGTCATCAGCTGGAGGGGAGCGGTGATCGAGCCTGAGCAGGGCACCGAG AGACACAT CCAGCGGGGACCACCT CACCTGCAGATT AGACCCCCAAGCCCAAGACCT GAAGGA CTCCTCAGAAGGCGGACACCGACCCTGAGAACTTACCTGAGATTTCGTCACAGAAGACACAA agagcagaagatgaggccagaaattgctgggttaaaaccagcaaatccaccccttaccag GGACTCCTCTTCTACATCAACTTGGCTGACCATTGGAAAGCTCTGGCTTTCAGGCTAGAGGA AGCAACTGTCGAGATTGCAGCGGAATATGATTCTCTTCCTCCTTGCCTTTCTGCTTTTCTG1 CTTTGGCGAGAGCTNTGACAACAGCAAGAGTTGGCGGCGGCGCTCGTGCTGGAGGAAAATGGA GTAGTCATGTACCCACCGCCGCCGCCGCCGCCTCATCGGGACTTCATCTCGGTGACGCTGAC GCGGGCTGTTGACGGCGCTGCG<mark>ATG</mark>GCTGCCTGCGAGGGCAGGAGAAGCGGAGCTCTCGGT CCTCTCAGTCGGACTTCCTGACGCCGCCAGTGGGCCGGGGCCCCTTGGGCCGTCGCCACCAC

FIGURE 10

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56529
><subunit 1 of 1, 699 aa, 1 stop</pre>

><MW: 79553, pI: 7.83, NX(S/T): 0

Important features of the protein: Transmembrane domain:

amino acids 21-40 and 84-105 (type II)

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FIGURE 1

GCACGACGTTGACCTGCTCCCTCTCAACGAGGAGCTGGACTATGGCTTTCCTGAGGCTGGGC GCAGGAAGAAGATCCGGCACCACATCTACGTGCTCAACCAGGTGGACCACTTCAGGTTCAAC CCTGCACTGTCCTCAACATCATGTTGGACTGTGACAAGACCGCCACACCCTGGTGCACATTC GCCCTTCCGCGAACGCTTCGAGGAGCTCCTGGTCTTCGTGCCCCACATGCGCCGCTTCCTGA CCGCCCCTGAGCACTGGGAAGAAGACGCATCCTGGGGGCCCCCACCGCCTGGCAGTGCTGGT *палаллалалалалалалалалалалалалалала*лал GGACCCCCCTGCCTTCCTGCTCACCCTACTCTGACCTCCTTCACGTGCCCAGGCCTGTGGG CAAGGCCTCAGGTCGTGGGCCCAGCTCTGACAGGATGTGGAGTGGCCCAGGACCAAGACAGCA GCCCTCGGGAATCACAACTGGGTACAAGACATTTCGCCACCTGCATGACCCAGCCTGGCGG CTGGGGCCGCGAGGACGACGAGTTCTACCGGCGCATTAAGGGAGCTGGGCTCCAGCTTTTCC ATCCTGCTGCTCCAAGCAGCACCTACCGGCTGTGCAATGGGATGTCCAACCGCTTCTGGGG CCTTCCACGTGGCCTCCCGGGAGCTCCACCCTCTACCACTACAAGACCTATGTCGGCGGC CGGGCAGCGCTCATCAACGTGGGCTTCCTCGAGAGCAGCAACAGCACGGACTACATTGCCAT TAGTGGGGAGGGCTGAACAGGACAACCTCTCATCACCCTACTCTGACCTCCTTCACGTGCCC AGCTACGCAATTGCAGCCACCCGGCCGCCAAGGCAGGCTTGGGCTGGGCCAGGACACGTGGG agc<u>tga</u>gctggatggacagtgaggaagcctgtacctacaggccatattgctcaggctcagga CTGCCTCTCGCTGGGCTTCTTCTCCCTACTCTGGCTGCAGCTCAGCTGCTGCTGGGGACGTGG AGGTCCGGGTTGCTCTCCGGCXGCCTCCCTCGGAAGTGTTCCGTCTTCCACCTGTTCGTGGC CGCCTCTCCGCACG<u>ATG</u>TTCCCCTCGCGGAGGAAAGCGGCGCAGCTGCCCTGGGAGGACGGC

FIGURE 12

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><subunit 1 of 1, 327 aa, 1 stop
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RHHIVTLNQVDHFRFRNAALINVGFLESSNSTDYIAMHDVDLLPLNEELDYGFPEAGPFHVA
SPELHPLYHYKTYVGGILLLSKQHYRLCNGMSNRFWGWGREDDEFYRRIKGAGLQLFRPSGI
TTGYKTFRHLHDPAWRKRDQKRIAAQKQEQFKVDREGGLNTVKYHVASRTALSVGGAPCTVL
NIMLDCDKTATPWCTFS
```

```
Signal peptide:
amino acids 1-42
```

```
Transmembrane domain:
amino acids 29-49 (type II)
```

N-glycosylation site.

amino acids 154-158

```
cAMP- and cGMP-dependent protein kinase phosphorylation site.
amino acids 27-31
```

```
Tyrosine kinase phosphorylation site.
```

```
amino acids 226-233
```

```
N-myristoylation site.
amino acids 19-25, 65-71, 247-253, 285-291, 303-309, 304-310
```

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FIGURE 13

FIGURE 14

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56862

<subunit 1 of 1, 73 aa, 1 stop</pre>

<MW: 7879, pI: 7.21, NX(S/T): 0

MLLLTLLLLLLLKGSCLEWGLVGAQKVSSATDAPIRDWAFFPPSFLCLLPHRPAMTCSQAQ PRGEGEKVGDG

Important features:

Signal peptide:

amino acids 1-15

Growth factor and cytokines receptors family:

amino acids 3-18

14/270

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FIGURE 15

TCCTTTCCAGTGCATGCCTTCATATATTGATCAGGACATGCAAGTGTTGTGGTATCAGGATG
GGAGAATAGTTGAAACCGATGAATCGCAAGGTATTTTGTTGTAAAAAGAACATGATTCACAAC
TGCTCCTTGATTGCAAGTGGCCTAACCATTTCTAATTTTGTTGGATCTACTACTATTTAATTTTTTGTGGATTTGTGGTATTTGTGGTATTTAG
GGGCTGTTCATGTCCAGACCAAACCTGGGAATAATACAACAACAAAAGGTGGACTTTCAGATTGA
AGAGTTCTGCACACACCAAACCTGCGAAGAGGGGTGTAAACAACAAAAGGTGACTTCAGATTG
AGAGTTCTGCACAGTACTTCCAGAGAGAGGGTGTTAAACAACAAAACCCCATGGCAATTG AAAGATTTTTTTTTGCAGGAAGATAGGTATTATTGCTTTTTGCTACTGTTTTTAAAGAAAACTA ACCAGGAAGAACTGCATTACGACTTTCAAGGGCCCTAGGCATTTTTTGCCTTTTGATTCCCTTTT AAGACTATTTACAGI<u>TAA</u>ATTAGAATGCTCCAAATGTTCTGCTTCGCAAAATAACCTTATTA GAGCTCACGTTTATTCAACATATTCACCCAATATTGCTCTGGAAGCTTATGTCATCAAGTCT GACAAACAATCGAATAGGATGTCTGAATGCAGACATATTTCGAGGACTCACCAATCTGGTTC GAGCATGTCCGCGCCGGGGAAGGCCCGTCCTCCGGCCGCCATAAGGCTCCGGTCGCCGCTGC TTTTCACTTAGCTTTCTGTGGGCATGTGTAATTGTATTCTCTGCGGTTTTTAATCTCACAG GACTACACTGTATTGAAGCAAATAGAGGAGGCACAACTCCAGCACCCTAATGGAACCACATT GATTTTAAGACAATAAGATGTTTTCATGGGCCCCTAAAAGTATCATGAGCCTTTGGCACTGC GCAATGTTTCAAATACATTTTCGAGTCTGGCACTAAAGGTATGTTACATTCTGCAATCATTT actiticggattatgggaggcgggatccabbagggaaacctggataagcagctgagctttaagt TTGAAAAATTTGGAAGATTTACCAAGGAGGAAAAATCAAAAGAGCTAGGTGACGTGATGGTT TTACACTGTGGAAGCAGCCAACTTTTCTGACAAAATGGATGTTATATTTGTGGCAGAAATGA ATGTTTAATCAGATGCCCCTCAATCTTACCAATGCCGTGGCAACAGCTCGACAGTTACTGGC TTTGGGCAGATGATGATTATTCTCGCTGTCAGTATGCAAATGATGTCACTAGAGTTCTTTAT GATATATCCCGGAAACCCACAGGATGAGAGAAAAGCTTGGCGCAGATGTGATAGAGGTGGCT GAATTGCCGTCTTTCTACATGACTCCATCTCATCGCCAAGTTGTGTTTGAAGGAGACAGCCT CACTGCAGGCCCAACCAGTCACAGGCGTGAAGCAGGAGCTGTTGACATGCGACCCTCCGCTT gcat cgctgggtaaaggagaagaacatcacggtacgggataccaggtgtgtttatcctaagt TCATTACGGT CTTTGGAATTCCAGACTGAGTATCTTTTGTGTGACTGTAACATACTGTGGAT GGCTAAACCTTTCGGGGAATTTGTTTTCTTCATTATCTCAAGGAACTTTTGATTATCTTGCG CTTATTAGTAGTATAGATCCAGGTGCCTTCTGGGGACTGTCATCTCTAAAAAGATTGGATCT AGCTGAAGAATGGCTCATTTTCTGGGTTAAGTCTCCTTGAAAGATTGGACCTCCGAAACAAT SCCSCCGCTGTTGCTCCCCCTCTCGCTGTTAGCGCTGCTCGCGCTGCTGGGAGGCGGCGGCGCC CTCGCCCGCAGGCCCCGCCCCGCAGC<u>ATG</u>GAGCCACCCGGACGCCGGCGGGGCCGCGCGCG GGGACCCATGCGGCCGTGACCCCCGGCTCCCTAGAGGCCCAGCGCAGCCGCAGCGGACAAAC TTGAAGCAAGCAAAATGAAAGCATTTTTACTGATTTTTAAAATTGGTGCTTTAGATATATTT atcaaaatttttggcagaaaacacaaatatgtcatatatctttttttaaaaaaagtattca CTTCACATAAAATATCAGAAATTACATTTATAACTGCAGTGGTATAAATGCAAATATACT ACTGGCTTCACGGGGATGACCTGTACCGTGTTCCAGAAAGTGGCAGCCTCTGATCGTACAGG GCCCCAGATACTCTGCCCAACCGCACGGTCACCCTGATTCTGAGTAACAATAAGATATCCG AGGGCGGCGGCGCCGCCGAGGGCAAGGTGGTGTGCAGCAGCCTGGAACTCGCGCAGGTCCT гт gaat gaat gaac gaaaaaaaaaaaaaa

FIGURE 16

EYLLCDCNILMMHRWVKEKNITVRDTRCVYPKSLQAQPVTGVKQELLTCDPPLELPSFYMTP VVCSSLELAQVLPPDTLPNRTVTLILSNNKISELKNGSFSGLSLLERLDLRNNLISSIDPGA VFQKVAASDRTGLSDYGRRD?EGNLDKQLSFKCNVSNTFSSLALKVCYILQSFKTIYS DERVLMLAQREAKACSRIVQCLQRIATYRLAGGAHVYSTYSPNIALEAYVIKSTGFTGMTCT TNAVATARQLLAYTVEAANFSDKMDVIFVAEMIEKFGRFTKEEKSKELGDVMVDIASNIMLA YLQCTRNTHGSGIYPGNPQDERKAWRRCDRGGFWADDDYSRCQYANDVTRVLYMFNQMPLNL SHRQVVFEGDSLPFQCMASYIDQDMQVLWYQDGRIVETDESQGIFVEKNMIHNCSLIASALT ${\tt FWGLSSLKRLDLTNNRIGCLNADIFRGLTNLVRLNLSGNLFSSLSQGTFDYLASLRSLEFQT}$ MEPPGRRRGRAQPPLLLPLSLLALLAGGGGGGGAAALPAGCKHDGRPRGAGRAAGAAEGK ISNIQAGSTGNWGCHVQTKRGNNTRTVDIVVLESSAQYCPPERVVNNKGDFRWPRTLAGITA

Signal peptide:

amino acids 1-33

Transmembrane domain:

amino acids 13-40 (type II)

N-glycosylation site.

433-437, 453-457, 592-596 amino acids 81-85, 98-102, 159-163, 206-210, 301-305, 332-336,

N-myristoylation site.

57-63, 99-105, 123-129, 142-148, 162-168, 317-323, 320-326 amino acids 29-35, 30-36, 31-37, 32-38, 33-39, 34-40, 51-57, 384-390, 403-409, 554-560

> WO 00/12708 PCT/US99/20111

FIGURE 17

TGGATAGTAGCATCCACCTGAGTAGTCTGATCAGTCGGCATGATGACGAAGCCACGAGAACA GTGTGGGCAGACACTTTTTGGAAGAGTCTGTCTGGGTGATCCTGGTAGAAGCCCCCATTAGGG AATAAAGGACAGTGGGTCATATAAGTTACTGCTTTCAGGGTCCCTTATATCTGAATAAAGGA GGAGAGTAGCTTAGTAGTATCTTCATCTTTTTTTTTTGGTCACTGTCCTTTTAAACTTGATCA TTTTGACTGAGCAACTTGAAGCAGAAAGAGAGAGATGTTATTGGCAAAAGGATCTCAAAAA CAGAGACATTGAGAGGCAANTTCGGAAAAAACAAAACATTCGTCTTTTGGGAGAACAGATTA ACAGTGGCCGGCGTACATGTGAAGCAGCAGTGGGACCAGCAGAGGCTTCGTGACGGAGTTAT GCGTGGGGATGTCTAGGAGCTCGAAGGTGGTGCTGGGCCTCTCGGTGCTGCTGACGGCGGCC

FIGURE 18

MSRSSKVVLGLSVLLTAATVAGVHVKQQWDQQRLRDGVIRDIERQIRKKENIRLLGEQIILT EQLEAEREKMLLAKGSQKS

Signal peptide: amino acids 1-21

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FIGURE 19

CCCOGCCTGGCACTCAGCCTTGCCAGAGATTYGGCTCCAGAATTTTTTGCCAGGCTTACAGAACAC ATTTGGAGGTCAGTAATTTCCAATGGGCGGGAGGCATTAAGCACCGACCCTGGGTCCCTAGG CTCTGTGTGTGTGTTTTGGGGGGTGGGGGTAGCTGGGGATTGGGCCCTCTTTCT CCAAGGGGCCCCATTGCCAAAGCATGCCTGCCCACCCTCGCTGTGCCTTAGTCAGTGTGTAC CCCACCTCCAAAGGTGCTGAGCTCACATCCACACCCCTTGCAGCCGTCCATGCCACAGCCCC TTCCACTCTTTTTTTCTCATCTCTTTTTCTGGGTTGCCTGTCGGCTTTCTTATCTGCCTGT CCCAGCCTCCCAAGTAGCTGGGAGGACAGGTGTGAGCTGCCGCACCCAGCCTGTTTCTCTTT TGCAGTGGTGCGATCTCAGCTCACTGCAACCCCCCCCCTCCTGGGTTCAAGCGATTCTCCTCC CTTTCTTTCTTTTTTTTTTTTTTTAAGACGGATTCTCACTCTGTGGCCCAGGCTGGAG TTCCTTCCTGTGTTTTGTTGCCCACATCCTGTTTTCACCCCTGAGCTGTTTCTCTTTTT CGTTCCCTCCAACCTCTTTGTTCTTCTTGCCCGAGTTTTCTTTATGGAGTACTTCTTTCC TGACCTGGTGCACTCTGCCCACCTGGTTTTTGTCAAGGTC<u>TAA</u>GACTCTCCCAAGAGGCTCC GCCTGGGACCGCCGACTGGCTGTGGCCATCCTGACGGCCATCAACCTACTGGCGTATGTGGC GCGGCCAGCCTCGGCGCTCGAGAGATGTAAGCTGCAGCCGCAGCCATGCCTACTACGTGTGT TGTCCTCCTATGCCACCGCCCTTGTTCTCTGGCCCCTCTACCAGTTCGATGAGAAGTATG GAGTGCACCAACGTGCTACCCATCCCCTTCCCCAGCTTCCTGTCGGGGGCTGGCCTTGCTGTC GCGTGGCCGTGTACGCCATCTGCTTCATCCTAGCGGCCATCGCCATCCTGCTGAACCTGGGG CATCATCTTCGCGTTCATCAGCGACCCCAACCTGTACCAGCACCAGCCGGCCCTGGAGTGGT ATCACTGGCTATATGGCCACCGTACCCGGGCTGCTGAAGGTGCTGGAGACCTTCGTTGCCTG CCTGCATCGCGTGTGTGGCTTACGCCACCGAAGTGGCCTGGACCCGGGCCCGGCCCAG CTATGTCCAGTTCCTGTCCCACGGCCGTTCGCGGGACCACGCCATCGCCGCCACCTTCTTCT ATCACCTTCGCCTGCTATGCGGCCTCTTCTGCCTCTCGGCCTCCATCATCTACCCCACCAC GGGGTCCATGGGCAACTGGTCCATGTTCACCTGGTGCTTCTCCCTTCTCCGTGACCCCTGATCA CTGCTGCAGCTGGTGTCTACCTGCGTGGCCTTCTCGCTGGTGGCTAGCGTGGGCGCCTGGAC GCTGCCATGCCAGTGACGGTAACCCGCACCATCACAACCACCACGACGTCATCTTCGGG CAAGTGTGGCTTAATCCGTCTCCACCACCAGATCTTTCTCCGTGGATTCCTCTGCT/AAGACC CTGTGGTATGAAAAAG CCACTGCCTAGAGGCCATCTTAAAGGAAGCAGGGGCTGGATGCCTTTCATCCCAACTATTCT TCTICATCGTGGAGCTGTGCGGGCTCCAGGCCCGCTTCCCCCTGTCTTGGCGCAACTTCCCC CCTGGGGTCCCCATGATCGTGGGGTCCCCTCGGGCCCTGACACACCCCCTGGGTCTCCTTCGC CTGTCGTCTTTGCTTCAGCCGCAGTCGCCACTGGCTGCCTGAGGTGCTCTTACAGCCTGTTC

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FIGURE 20

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58727
<subunit 1 of 1, 322 aa, 1 stop
<MW: 35274, pI: 8.57, NX(S/T); 1</pre>

MPVTVTRTTITTTTSSSGLGSPMIVGSPRALTQPLGLLRLLQLVSTCVAFSLVASVGAWTG
SMGNWSMFTWCFCFSVTLIILIVELCGLQARPPLSWRNFPITFACYAALFCLSASIIYPTTY
VQFLSHGRSRDHAIAATFFSCIACVAYATEVAWYRARPGEITGYMATVPGLLKVLETFVACI
IFAFISDPNLYQHQPALEWCVAVYAICFILAAIAILLNIGECTNVLPIPFPSFLSGLALLSV
LLYATALVLWPLYQFDEKYGGQPRRSRDVSCSRSHAYYVCAWDRRLAVAILTAINLLAYVAD
LVHSAHLVFVKV

Important features:

Transmembrane domains:

amino acids 41-60 (type II), 66-85, 101-120, 137-153, 171-192, 205-226, 235-255 and 294-312

N-glycosylation site.

amino acids 66-69

Glycosaminoglycan attachment site.

amino acids 18-21

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FIGURE 2

TENANCISCIANCINCOCANCINATITION TITIATIANANAINGGGTTICACCATUTIQGCCAAGCIGGT
TENANCISCIANCICCANCINCOCANCIN

FIGURE 22

MFLATLSFILLFFAHPFGTVSCEYMLGSPLSSLAQVNLSPFSHPKVHMDPNYCHPSTSLHLCS
LAMSFTRILHPPLSPGISQVVKDHVTKPTAMAQGRVAHLIEWKGWSKDSDSPAALESAFSSY
SDLSEGEQEARFAAGVAEQFAIAEAKLRAWSSVDGEDSTDDSYDEDFAGGMDTDMAGQLPLG
PHLQDLFTGHRFSRPVRQGSVEPESDCSQTVSPDTTLCSSLCSLEDGLLGSPARLASQLLGDE
LLLAKLPPSRESAFRSLGPLEAQDSLYNSPLTESCLSPAEEEPAPCKDCQPLCPPLTGSWER
QRQASDLASSGVVSLDEDEAEPEEQ

Signal peptide:

amino acids 1-15

Casein kinase II phosphorylation site.

amino acids 123-127, 128-132, 155-159, 162-166, 166-170, 228-232, 285-289, 324-328

Tyrosine kinase phosphorylation site.

amino acids 44-52

N-myristoylation site.

amino acids 17-23, 26-32, 173-179

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 11-22

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FIGURE 2

CAATGACTGCATTCAACGGGGCCATGGCAGGAAAGCTGACCCTACCCAGGAAAGTAATAGCT GACATAGCCCAGAGTTTCTGTTATTGGGAAATTGAGGCAATAGAAATGACAGACCTGTATTC ACAATGAAGATGACTCTTTACTGCTCTGCCTGAAGCCCCTAGTACCATAATTCAAGATTGCAT CCAAAGGTTTTCTTTACAATTTTTGGCCATCCTGAGGCATTTACTAAGTAGCCTTAATT TTTGTCAAGGAGAATCATAAAAGCAGGAGACCAGTAGCAGAAATGTAGACAGGATGTATCAT CATCCTAGCCTTTTGACAAATTCATCTTTCAAAAGGTTACACAAAATTACTGTCACGTGGAT TCCACTTCGTACTTCTGTA<u>TAG</u>AACTAACAGCAAAAAGGCGTTAAACAGCAAGTGTCATCTA GATTCAGCCATGCCAGAAAGTGAAGAAAATGCACGTGATGGCATTCCTATGGATGACATACC GGATTCATTTTCCCATCGGCGACTTTATGACGACAGAAATGAACCAGTTCTGCGATTAGACA TCTTTAAAAGTCTTCAAAGGTTTTGGGAATTTTAACTTGTCTTAATATATCTTAGGCTTCAA TAGTACGTTATAATTTTCTAGATCAGCACACACATGATCAGCCCACTGAGTTATGAAGCTGA TTTCTTAAATGAAAATTGAAAGGGTGCTTTTTAAAGAAAATTTTGACTTAAAGCTAAAAAGAG TCACCATTACAGCCCTGCCTCATAACTAAATAATAAAAATTATTCCACCAAAAAATTCTAAA TGTATTTTAGTAGTATTTTCTTAGTAGAAAATATTTGTGGAATCAGATAAAACTAAAAGATT ATSCACCGGAACCTTATGATGTGAGTTTTTGGGAATTCTAGCTACTACAATCCAACTTTGAAT GCTATTCTGGGTGTCTCATTGCTTACTCTTGTGGGCTACTTGTTGTGTGGAAAAAGGAAAAC ATACGTCAGATCCCCAAAAAGAAAATAGAAATACAGGAATAGTATTCGGGGCCATTTTAGGT TCAAGAAAAAACAACTCTACAGCCTACCTTAAAATTCACCAATAATTCAAAAACTCTTTCCAA ATAGTGGAACCAAGTGGATGGCTTACCACAAACAGTGATAGCTTCACTGGGTTTACCCCCTTA ACAGTTCCATTACAGTTAGCATCCTCTCTTCAGAACCAACTTCTCCATCTGTGACCCCCTTG CAGCCACGGAATAACAGATTTCTCCAGTAACTCATCAGCAGAGCATTCTTTGGGCAGTCTAA TTATTTGGGTGCCTTAAAAACTCAATGAGAATCATGGT TGCTCTCTTCAGAAAACTTCACTTGGTCTTTGGTCAATGACACCGTGAAAACTCCTGATA TGGAATGCACCTATAGCAGATGAAGATCTTTTGCCCATCTCAGCACATCCCAATGCTACACC AACCCACATCTACCATTTCCACAAGCCCTCCCTTGATCCATAGCTTTGTTTCTAAAGTGCCT GAAAATATAACCACCTCAAATCTCAAGGCGAGTCATTCCCCTCCTTTGAATCTACCCAACAA TTAAAACAATGGAAAATAAACCTATTTCTTTGGAAAGTGAAGCAAACTTAAACTCAGATAAA ATCGGGGAGCCATGGAAAAGAAAATCAAGACATAAACACAACACAGAACATTGCAGAAGTTT AMGCCTACA<u>ATG</u>TTGGCCTTAGCCAAAATTCTGTTGATTTCAACGTTGTTTTATTCACTTCT CCTGAAGCTTCTGTTACTAGCCATTGTGAGCTTCAGTTTCTTCATCTGCAAAATGGGCATAA CAGATTCCTTTCAGACAGGACAACTGTGATATTTCAGTTCCTGATTGTAAATACCTCCTAAG GGCACCCTCCTGCTCAGTGCGACATTGTCACACTTAACCCATCTGTTTTCTCTAATGCACGA

FIGURE 24

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58732
><subunit 1 of 1, 334 aa, 1 stop
><subunit 1 of 1, 334 aa, 1 stop
><MM: 36294, pI: 4.98, NX(S/T): 13
MLALAKILLISTIFYSLLSGSHGKENQDINTTQNIAEVFKTMENKPISLESEANLNSDKENI
TTSNLKASHSPPLNLPNNSHGITDFSSNSSAEHSLGSLKPTSTISTSPPLIHSFVSKVPWNA
PLADEDLIPISAHDNATBALSENFTWSLVNDTVKTPDNSSITVSILSSEPTSPSVTPLIVE
PSGWLITINSDSFTGFTPYQEKTTLQPTLKFTNNSKLFPNTSDPQKENRNTGIVFGAILGAIL
GVSLLTLVGYLLCGKRKTDSFSHRRLYDDRNEPVLRLDNAPEPYDVSFGNSSYYNPTLNDSA
MPESEENARDGIPMDDIPPLRTSV</pre>

Signal peptide: amino acids 1-23

Transmembrane domain: amino acids 235-262

amino acids 235-262

W-glycosylation site.

amino acids 30-34, 61-65, 79-83, 90-94, 148-152, 155-159, 163-167, 218-222, 225-229, 298-302, 307-311

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FIGURE 25

AATGCACAAAATTGTGTAGGTGCTGAATGCTGTAAGGAGTTTAGGTTGTATGAATTCTACAA TCAGATCTCAACATIGTTGGTTTCTTTTGTTTTTCATTTTGTACAACTTTCTTGAATTTAGA GTGGAGCAATTTTAAAATTTGAAATATTTTAAATTGTTTTTGAACTTTTTGTGTAAAATATA GGTTTAGATTTCTGAAAGCAGCATGAATATATCACCTAACATCCTGACAATAAATTCCATCC AAAAAAGGAAAAAAAAAAAAACTACTAACCACTGCAAGCTCTTGTCAAATTTTAGTTTAAT CATTAAGGTTTATGGGATACTCAAGATATTTACTCATGCATTTACTCTATTGCTTATGCTTT AAGAGGCAACAGATAGAGTGTCCTTGGTAATAAGAAGTCAGAGATTTACAATATGACTTTAA ATGCTGGAAGATTAGACACTTCCCCAACGAATTTATTGTTGAGACCAAGATCTGTCAAGAG ${f r}$ CAAACTGGCGAGTGGCAGATATCTGCCTCAAACTTATGTGGTTCGAGAAGACCTAGTTGCTG TATCTGATGCCCCTCAATACTTCTATTGTTATGCCTCCAAAAAATCTGGTAGAGCTCTTTGG CAATTATTCATGACTTTGAAAAGGGAATGACTGCTTACCTGGACTTGTTGCTGGGGAACTGC GGATGACAACATTGCAATCATTGATGTGCCTGTCCCCAGTTTCTCTGATAGTGACCCTGCAG AATTCCCTTCGTGGAGGAGAGCCTAACTTCCTGCCTGTGACTGAGGAGGCTGACATTCGTGA TCATGCCCAAGAGCACCATTTACCGTGGAGAGATGTGCTTTTTTTGATTCTGAGGATCCTGCA CTTAGGCCTTTCATTCATCTTGGCAGGACTTATTGTTGGTGGAGCCTGCATTTACAAGTACT AAGGAGCTCCGAGTTGCCACCCAGGAAAAAGAGGGCTCCTCTGGGAGATGTATGCTTACTCT AGCCCGAAGATTCACT<u>ATG</u>GTGAAAATCGCCTTCAATACCCCTACCGCCGTGCAAAAAGGAGG AACAGGATCTCCTCTTGCAGTCTGCAGCCCAGGACGCTGATTCCAGCAGCGCCTTACCGCGC AATTACATCTTTGCAGTTCTGTTAGGTGCTCTGTAATTAACCTGACTTATATGTGAACAATT GTTGTTTTTTTTTGTTTGTTTTTTTTTTTTTTTAAGTAAGCTCTTTATTCATCTTATG TGGCATTGCTTGTTTTTGAAACTGAAATTACATGAGTTTCATTTTTTTCTTTGCATTTATAG AAGTCCTTCCGCCTTCGTCGCAGAGACCTCTTGCTGGGTTTCAACAAACGTGCCATTGATAA AGGCGCGGCAAGACGTGGAGGCCCTCCTGAGCCGCACGGTCAGAACTCAGATACTGACCGGC

FIGURE 26

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58828
<subunit 1 of 1, 263 aa, 1 stop</pre>

<MW: 29741, pI: 5.74, NX(S/T): 1

MVKIAFNTYTAVQKEEARQDVEALLSRTVRTQILTGKELRVATQEKEGSSGRCMLTLLGLSF ILAGLIVGGACIYKYFMPKSTIYRGEMCFFDSEDPANSIRGGEPNFLPVTEEADIREDDNIA IIDVPVPSFSDSDPAAIIHDFEKGMTAYLDLLLGNCYLMPLNTSIVMPPKNLVELFGKLASG

IIDVPVPSFSDSDPAAIIHDFEKGMTAYLDLLLGNCYLMPLNTSTVMPPKNLVELFGKLASG RYLPOTYVVREDLVAVEEIRDVSNLGIFIYQLCNNRKSFRLRRDLLLGFNKRAIDKCWKIR HFPNEFIVETKICQE

Type II transmembrane domain:

amino acids 53-75

N-glycosylation site. amino acids 166-170

Casein kinase II phosphorylation site. amino acide 35-39, 132-136, 134-138

N-myristoylation site.

amino acids 66-72, 103-109

Prokaryotic membrane lipoprotein lipid attachment site. amino acids 63-74

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FIGURE 2'

CTGGCAGGAGGTCCTCTCCCCCATCCCTCCATCTGGGGCTCCCCCAACCTCTGCACAGCTCT CCCAGCCTGGAGCAGGGGGGCCCTGGCCACCCCTGTTGCTCACACATTGTCTGGCAGCCTG CCTGTGTTTGAGGGGACCTCCACCCTGGGGAAGTCCGAGGGGGCTGGGGAAGGGTTTCTGACG GATCAGGTTGAATGAATGGAACTCTTCCTGTCTGGCCTCCAAAGCAGCCTAGAAGCTGAGGG GCTACAGGGTAAAATCCTGCAGCACCCACTCTGGAAAATACTGCTCTTAATTTTCCTGAAGG CCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGTGCCCGGCCCAAACTACTTTTTAAAACA ACAGCTCCCCTGACAAAGTGAGGGAGGGCACGTGTCCCTGTGACAGCCAGGATAAAACATCC GGAATCTTACCAAGTGCCATCATCCTTCACCTCAGCAGCCCCAAAGGGCTACATCCTACAGC TGCCAATCCCAGCATGTGCTGATTCTACAGCAGGCAGAAATGCTGGTCCCCGGTGCCCCGGA TGTCTAACAGTCCTCCCGGGCTGCCAGCCCTGACTGTCGGGCCCCCAAGTGGTCACCTCCCC GAAGCCCAGGGACCAGTGGGTCCCCCGAAAGCCCCTGTGCTTGCAGCAGTGTCCACCCCAG GGGACATGGGGTCCCAGTGGAGACACCAGAGGCGGAGGAGGAGCCGTGCTCAGGGGTCCTTG ©TGGACCAGAGTGACCGGGCCCGGGGCCCCCGGGCCTTCAGTGAGGTCCCCGACAGAGCCCC GCTGATTGCTGTGGGGCTCCCTGGCCTTTCTGCTGATGTTCATCGTCTGTGCCGCGGTCA CGCCACCTGGACCCCGGCCTCAGCCCCACATCGATGGGGCCCCAGACACCCACAACCCTGGGG TCAAGCGCTCTCCAAGCACCCCCGGCCTGGGGGTGAGTTTCTCATCCCGCTACTGCTGCTGG TGGCCCCCTGTTTCTAGTTGGTCCAGGATTAGGGATGTGGGGTATAGGGCATTTAAATCCTC AGGGGCTGTGGTGGCCGGTGAGGGCCAAGGGGAGCTGGAAGGGTCTCTCTTGTTAGCCCAG CGACAGCNGGCCCGAGGAAGCCCTGGATTCCTCCCGGCAGCTCCAGGCCGACATCTTGGCCG GGCCCATCACCCCCCCACCAACTTCCTGGATGGGATAGTGGACTTCTTCCGCCAGTACGTGAT CCTGGAGGATGTGGCGGGTAGTGGGGAGGCCGAGGGCTCGTCGGGCCTCCTCCCCGAGCCTCC TGTCCACAATATTCGTCAGTCCTCGACAGGGAGCCTGGGCTCCGTCCTGCTTTAGGGAGGCT TCACCCGGCAGAAGCAGAAGGCCTCGGCCTATTACCCCATCGTCCTTCCCCCAAGAAGAAGTAC TIGCTGCTGCGGGGTCTGTGCCTGCTACCGACGCCCCCTGTGCCCCCTGAAGGCCACGTT AAGGAACTGGTCCTGGGGGCACC<u>ATG</u>GTTTCGGCGGCAGCCCCAGCCTCCTCATCCTTCTG CTTCCAGCCCAGGTGCCCCCCACTCTCGCTCCATTCGGCGGGAGCACCCAGTCCTGTACGCC GGAGGAGGGAGGGCGGCAGGCGCCAGCCCAGAGCAGCCCCGGGCACCAGCACGGACTCTCT

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FIGURE 29

EIGURE 28

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58852
><subunit 1 of i, 283 aa, 1 stop</pre>

><MW: 29191, pI: 4.52, NX(S/T): 0

MVSAAAPSILIILLILIGSVPATDARSVPLKATFLEDVAGSGEAEGSSASSPSLPPPMTPAL
SPTSMGPQPTTLGGPSPPTNFLDGIVDFFRQYVMLIAVVGSLAFILMFIVCAAVITRQKQKA
SAYYPSSFPKKKYVDQSDRAGGPRAFSEVPDRAPDSRPEEALDSSRQLQADILAATQNLKSP
TRAALGGGDGARMVEGRGAEEEEKGSQEGDQEVQGHGVPVETPEAQEEPCSGVLEGAVVAGE
GQGGLEGSILLIAQEAQGPVGPPESPCACSSVHPSV

Signal peptide: amino acids 1-25

Transmembrane domain: amino acids 94-118

N-myristoylation site. amino acids 18-24, 40-46, 46-52, 145-151, 192-198, 193-199 211-217, 238-244, 242-248

GAGGACAGGGAGTTTCCAGCAACATGAGGGAAATAAGCAAAGAGGGGCAATCGCCTCCTTGGA AGCTCTCGCATCCCG<u>TGA</u>CCTCCAGACAAGGAGCCACCAGATTGGATGGGAGCCCCCACACT GGAAGAATTTTAAATCCAAGCTGGGTTTCATCAACTGGGATGCCATAAACAAGGACCAGAGA TGGTGGAGTCAATACTGTGAACTCTGAGACGTCTCCTGGGATGTTTAACTTTGACACTTTCT GGCTCTGGAGACAATTATCGGGGGCAAGGGTCGAGCTGGGGGCAGTGGAGGAGGTGACGCTGT CGGGTGTGAAAAGCCAGGGAATGAAGCCCGCGGGAGCGGGAATCTGGGATTCAGGGCTTCA TCCAGCACCGGCTCCTCCGGCAACCACGGTGGGAGCGGCGGAGGAAATGGACATAAACC GTGGCAGCAGTGGCAACAGTGGTGGCAGCAGAGGTGACAGCGGCAGTGAGTCCTCCTGGGGA TGGCAGCAGCAGTGGCAGCAGTGGCAGCAGTGGCGGCAGCAGTGGCGGCAGCAGTG GCACGAATCCCCCACCATCTGGCTCAGGTGGAGGCTCCAGCAACTCTGGGGGAGGCAGCGGC TCAGGGAGCTGTGGCCAGCCTGGCTATGGTTCAGTGAGAGCCAGCAACCAGAATGAAGGGT CCTCAGGGAGCTCCCTGGGGTCAAGGAGGCAATGGAGGGCCACCAAACTTTGGGACCAACAC AGGCCATGGCATCTTTGGCTCTCAAGGTGGCCTTGGAGGCCAGGGCCAGGGCAATCCTGGAG GATGCTGTCCCCGGCTCCTGGCAGGGGGTGCCTGGCCACAGTGGTGCTTGGGAAACTTCTGG CTCTGGGAAACACTGGGCACGAGATTGGCAGACAGGCAGAAGATGTCATTCGACACGGAGCA GCAGGTTCCAGGCTTTGGCGCAGCAGATGCTTTGGGCAACAGGGTCGGGGAAGCAGCCCATG GGCTCTAAAGTCAGTGAGGCCCTTGGCCAAGGGAACCAGAGAAGCAGTTGGCACTGGAGTCAG CCCTCCTTAAAACACCACCCTCTCATCACTAATCTCAGCCCTTGCCCCTTGAAATAAACCTTA TCACAGTCGGGCAGCAGTGGCAGTGGCAGCAATGGTGACAACAACAATGGCAGCAGCAGTGG TGGGAGACGCCCTGAGCGAAGGGGTGGGAAAAGGCCATTGGCAAAGAGGCCGGAGGGGCÇAGCT CCCCTGCAGAGCGGAGAGGAAAGCACTGGGACAAATATTGGGGAGGCCCTTGGACATGGCC AAGTTCCAGGGGCCCCTGGCCTGCCTCCTGGCCCTCTGGCCTGGGCAGTGGGGAGGCTGG

PCT/US99/20111

FIGURE 30

><subunit 1 of 1, 440 aa, 1 stop ></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59212

><MW: 42208, pI: 6.36, NX(S/T): 1

GGSGDNYRGQGSSWGSGGGDAVGGVNTVNSETSPGMFNFDTFWKNFKSKLGFINWDAINKDQ GSSTGSSSGNHGGSGGGNGHKPGCEKPGNEARGSGESGIQGFRGQGVSSNMREISKEGNRLL GSQSGSSGSSGDNNNGSSSGGSSSGSSSGSSSGGSSGGSSGNSGGSRGDSGSESSW NPQGAPWGQGGNGGPPNFGTNTQGAVAQPGYGSVRASNQNEGCTNPPPSGSGGGSSNSGGGS ${f DD}{f NVRGSWQGVPGHSGAWETSGGHGIFGSQGGLGGQGQGNPGGLGTPWVHGYPGNSAGSFGM}$ agskvsealgogtreavgtgvrovpgfgaadalgnrvgeaahalgntgheigroaedvirhg MKFQGPLACLLLÄLCLGSGEAGPLQSGEESTGTNIGEALGHGLGDALSEGVGKAIGKEAGGA

Signal peptide:

amino acids 1-2:

N-glycosylation site.

amino acids 265-269

Glycosaminoglycan attachment site.

amino acids 235-239, 237-241, 244-248, 255-259, 324-328, 388-392

Casein kinase II phosphorylation site.

amino acids 26-30, 109-113, 259-263, 300-304, 304-308

N-myristoylation site.

amino acids 17-23, 32-38, 42-48, 50-56, 60-66, 61-67, 64-70, 74-80, 90-96, 96-102, 130-136, 140-146, 149-155, 152-158, 155-161, 159-165, 163-169, 178-184, 190-196, 245-251, 246-252, 248-244, 238-244, 239-245, 240-246, 245-251, 246-252, 249-252, 253-259, 256-262, 266-272, 270-276, 271-277, 275-281, 279-285, 283-289, 284-290, 287-293, 288-294, 291-297, 292-298, 295-301, 298-304, 305-311, 311-317, 315-321, 319-325, 322-328, 323-329, 325-331, 343-349, 354-360, 356-362, 374-380, 381-387, 3 383-389, 387-393, 389-395, 395-401

Cell attachment sequence.

amino acids 301-304

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GCCGTGCTTGGCGCCCTGGCGTGTGTCTAGCTGCTTCTTGCCGGGCACAGAGCTGCGGGCTCTGGGGGCACCGGGACACCGGAGCTCTGGGGCTCTGAGGGCCACCGGAGCACCCCTGAGGTGCTCTGAAGTGCTCCTGAGGTGCTCCTTAACCGACACCCCTGAGGTGCTCTGAAGTCCTAAGCTCCTGAGGAAACCTAAGCTC GTIATTTCACAACTGTCCTGCGACGTTGGCCTGGGCACGTCATGGAATGGCCCATGTCCCTCTGCTGCGGAGGCGTCGCCCCCGGAAGGC «ТСССТЕНТАЛЯСОСТТЕМАСТВОАСАСАВЛЯЮСССМАНАВИТИВОСТТВОАСАЛТБСВССТВТВОЯВАСОЛОЕ НОВТЕСТЕТИВАКОЛОЕ НОВТЕСТЕТИВАКОЛОЕ НОВТЕСТЕТИВАКОЛОЕ НОВТЕСТЕТИВАКОЛОЕ НОВТЕСТВОАКОЛОЕ НОВТЕСТВОАКОЛОЕ НОВТЕСТВОАКОЛОЕ НОВТЕСТВОАКОЛОЕ НОВТЕСТВО GACCGGTCCCTCCGGTCCTGGATGTGCGGACTCTGCTGCAGCAAGGCCTGCAGGCCGCCGGGCGATGCTCACCG ТGCCTGGCTGGTGGAGTTTCTCTCCCTTTGCTGACCATGTTGTTCCCTTGCTGGAATATTACCGGGACATCTTCA

FIGURE 32

MCFLNKLLLLAVLGWLFQIPTVPEDLFFLEEGPSYAFEVDTVAPEHGLDNAPVVDQOLLYTC
CPYIGELRKLLASWVSGSSGRSGGFWRKITPTTTTSLGAQPSQTSQGLQAQLAQAFFHNQPP
SLRRTVEFVAERIGSNCVKHIKATLVADLVRQAESLLQEQLVTQGEEGGDPAOLLEILCSOL
CPHGAQALALGREFCQRXSPGAVRALLPEETPAAVLSSAENIAVGLATEKACAWLSANITAL
IRREVKAAVSRTLRAQGPEPAARGERRGCSRA

Signal peptide: amino acids 1-18

N-glycosylation site. amino acids 244-248

cAMP- and cGMP-dependent protein kinase phosphorylation site.
amino acids 89-93

Casein kinase II phosphorylation site. amino acids 21-25, 167-171, 223-227

N-myristoylation site.

amino acids 100-106, 172-178, 207-213

Microbodies C-terminal targeting signal. amino acids 278-282

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FIGURE 33

CCACCACTGGCTACTCAGCTGATGTGGGCAACAAGACCACCTACCGCGTCGTGGCCCATTCC AACAAGACACTGCCCTCTCGGTGCCACCAGTGTGTGATTGTCAGCAGCTCCAGCCACCTGCT GCCGCCGACCTGTCAACCTCAAGAAGTGGAGCATCACTGACGGCTATGTCCCCATTCTCGC CATCCTCTACAGCTCCAACAGTGCCAATGAGGTCTTCCATTACGGCTCCCTGCGGGGCCGT AGTAGCAACAAAGAGCAGCGGTCAGCAGTGTTCGTGATCCTCTTTGCCCCTCATCACCATCCT AAGACTCTCTGCTTTTGCCACAGCAGTTCCTGCAGCTTCCTTGAGGTGTGAACCCACATCCC TCCCTTGACAGGTCTGGTGGCTGGTTCGGGGTCTACTGAAGGCTGTCTTGATCAGGAAACTC TGGGGAATCTGTTGGCGAATCAGGGATTTGGGAGTCTATGTGGTTAATCAGGGGTGTCTTTC
TTGTGCAGTCAGGGTCTGCGCACACTCAATCAGGGTAGAGGGGGTATTTCTGAGTCAATCTG
AGGCTAAGGACATGTCCTTTCCCATGAGGCCTTTGGTTCAGAGCCCCAGGAATGGACCCCCA
ATCACTCCCCACTCTGCTGGGATAATGGGGTCCTGTCCCAAGGAGCTTGGAACTTGGTGTT CTGGAGTGTCTCCCAGCCAATCAGGGCCTTGAGGAGGATGTATCCTCCAGCCAATCAGGGCC $exttt{TCACCTTCTCCACCCTCCTGGACCTAGGCCAGCCTGTGGGACCTCAGGAGGGTCAG}$ CAACCACCACCGCTTCATCACCGAGAAAAGGGTCTTCTCATCGTGGGCCCCAGCTGTATGGCA TACGAGCCCAAGGGGCCGGACGAATGTGTCACCTACATCCAGAATGAGCACAGTCGCAAGGG GCATGGTCCCCCCCAACTACTGCAGCCAGCGGCCCCGCCTCCAGCGCATGCCCTÁCCACTAC GAGCACAGGCTGGTTTACCATGGTGATCGCGGTGGAGTTGTGTGACCACGTGCATGTCTATG CAATTIGACGACCTCTTCCGGGGTGAGACGGGCAAGGACAGGGAGAAGTCTCATTCGTGGTT AGCGAGCGGGCCTGGTGTTCCCCAACATGGAAGCATATGCCGTCTCTCCCGGCCGCATGCGG <u>AGTGTGTTCCGCGTGCTGAGGAGGCCCCCAGGAGTTTGTCAACCGGACCCCTGAAACCGTGTT</u> TGCCCCCAGGGCCACCTGCAGGACGCCGACACCTACCCCTCAGCAGACGCCGGAGAGAA<u>ATG</u> GGTGTGTTTGTCTCCTGCTCTTCTGGAGCCTGGAAGGGAAAGGGCTTCAGGAGCAGGCTGTGA ATCACCTGGGTTCTGTCCCCTGGCTCTGTATCAGGCACTTTATTAAAGCTGGGCCTCAGTGG CTAGCAGGGAGGTTTTCCAACTGTTGGAGGCGCCTTTGGGGGCTGCCCCTTTGTCTGGAGTCA GCAAACTCCTTCAGGGTTGGGGGACTCTGAAGGAAACGGGACAAAACCTTAAGCTGTTTTCT CAGCTCTTTGGGGGGTCTGGGGTGACCTCCCCACCTCCTGGAAAACTTTAGGGTATTTTTGC GTGCCCTCGGGTCTGTCCTCCCGTCTGGACCCTCCCAGCCACTATCCCTTGCTGGAAGGCT GGCTGGCATCCAGGTCTTGGCTCTGCCCTGAGACCTTGGACAAACCCTTCCCCCCTCTCTGG CCCCTCAATTTCCAGCACCAGAAAGAGAGATTGTGTGGGGGTAGAAGCTGTCTGGAGGCCC AGGAGAAGCAGCCTCCGCCCAGCCGCTAGGCCAGGGACCATCTTCTGGCCAATCAAGGCTTG GGGCGGTGACTGCCCCAGACTTGGTTTTGTAATGATTTGTACAGGAATAAACACACCTACGC GGCTGGAGGGACCAGATGGAGGAGGCCAGCAGCTAGCCATTGCACACTGGGGTGATGGGTG CTGGGGGCTTCCGAGGGTCTCCCTCGACCCTCTGTCGTCCTGGGATGGCTGTCGGGAGCTGT TAGCCCCTCAGCCAGCTGCCATTAGCTTGGCTCTTAAAGGGCCAGGCCTCCTTTTCTGCCCT CACCCTTCTGCCCACACCAGTTTCCAGTGCGGAGTCTGAGACCCTTTCCACCTCCCCTACAA

FIGURE 34

RQFDDLFRGETGKDREKSHSWLSTGWFTMVIAVELCDHVHVYGMVPPNYCSQRPRLQRMPYH SSVFRVLRRPQEFVNRTPETVF1FWGPPSKMQKPQGSLVRVIQRAGLVFPNMEAYAVSPGRM GNKTLPSRCHQCVIVSSSSHLLGTKLGPEIERAECTIRMNDAPTTGYSADVGNKTTYRVVAH MSSNKEQRSAVFVILFALITILILYSSNSANEVFHYGSLRGRSRRPVNLKKWSITDGYVPIL YYBPKGPDECVTYIQNEHSRKGNHHRFITEKRVFSSWAQLYGITFSHPSWT

amino acids 1-29 Signal peptide:

amino acids 9-31 (type II) Transmembrane domain:

amino acids 64-68, 115-119 N-glycosylation site.

amino acids 50-54 cAMP- and cCMP-dependent protein kinase phosphorylation site.

amino acids 3-7, 29-33, 53-57, 197-201 Casein kinase II phosphorylation site.

amino acids 253-262 Tyrosine kinase phosphorylation site.

amino acids 37-43, 114-120, 290-294 N-myristoylation site.

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FIGURE 35

анасальноситествой деней выполнений в пределений в преде GTTTCTCATAGTTGGGGTCTTCTMAGGGAAAAACACTAAAATGAGGAACTCAGCBGACCGGGGAGCGACGCAGCTT GAGGGAAGCATCCCTAGCTGTTGGCGCAGAGGGGCGAGGCTGAAGCCGAGTGGCCCGAGGTGTCTGAGGGGCTGC

IGURE 36

SSPDEGSFLYTLPDDSTHQLLQPHHDCCQRQEQPAAVGQSGVRRAFDSPVLEAVWDPPFHSG CANGIHMNRGCPSAAVGYPGMKPQQHCPGELQQQSDTSSLLRQTHLGNGYDPQSHQITRGPK IIVTFIPFCLWRAWSKQKHTTDLGFPRSALPPSCPYTMVPLGGLPGHQASGQPYLSGISGR PIHGFYIYYRPTDSDNDSDYKKDMVEGDKYWHSISHLQPETSYDIKMQCFNEGGESEFSNVM RALNMLGESEPSAPSRPYVVSGYSGRVYERPVAGPYITFTDAVNETTIMLKWMYIPASNNNT TSVYVTWIPRGNGGFPIQSFRVEYKKLKKVGDWILATSAIPPSRLSVEITGLEKGTSYKFRV GQTAMVTFRTGRRPKPEIMASKEQQIQRDDPGASPQSSSQPDHGRLSPPEAPDRPTISTASE HEGSGRAP ILYYVVKHRKQVTNSSDDWTISGIPANQHRLTLTRLDPGSLYEVEMAAYNCAGE LGNPEQMLRGQPALPRPPTSVGPASPKCPGEKGQGAPAEAPIILSSPRTSKTDSYELVWRPF RRALRVLSMGPEDEGVYQCMAENEVGSAHAVVQLRTSRPSITPRLWQDAELATGTPPVSPSK AVILYNVQVFEPPEVTMELSQLVIPWGQSAKLTCEVRGNPPPSVLWLRNAVPLISSQRLRLS IVNASQEDEGMYKCAAYNPVTQEVKTSGSSDRLRVRRSTAEAARIIYPPEAQTIIVTKGQSI RMNVTWRLNGKELNGSDDALGVLITHGTLVITALNNHTVGRYQCVARMPAGAVASVPATVTI PPCCLGLVPVEEVDSPDSCQVSGGDWCPQHPVGAYVGQEPGMQLSPGPLVRVSFETPPLTI ICETKARKSSGQPGRLPPPTLAPPQPPLPETIERPVGTGAMVARSSDLPYLIVGVVLGSIVI ILECVASGIPPPRVTWAKDGSSVTGYNKTRFLLSNLI.IDTTSEEDSGTYRCMADNGVGQPGA ANLQDFKLDVQHVI EVDEGNTAVIACHLPESHPKAQVRYSVKQEWLEASRGNYLIMPSGNLQ ${ t MLRGIMTAWRGMRPEVILACLLLATAGCFABLNEVPQVIVQPASIVQKPGGIVILGCVVEPE}$

Signal peptide:

amino acids 1-30

Transmembrane domain:

amino acids 16-30 (type II), 854-879

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FIGURE 37

CCGCCTGGGCATGATGATAGATTTGTCCTATGCATCGGACACCTTGATAAGAAGGGTCCTGG CACATGTACACCAACGTCAGCGGATTGACAAGCTTTGGTGAGAAAGTAGTAGAGGAGTTGAA GGGTGCCCAGTTCTGGTCAGCCTCCGTCTCATGCCAGTCCCAGGACCAGACTGCCGTGCGCC CACCCCAAAACCCTGGACCTTCGGGGTCGCGCGCAGGCCCTGATGCGGAGTTTCCCCACTCG AGTTCATTCACAAGCATATGCTGAGAATAAACATGTTACACATGGAAAA TGC<u>TGA</u>CACAGTCGGTCCCCGCAGAGGTCACTGTGGCAAAGCCTCACAAAGCCCCCCTCTCCT CCCCATACCTTGTTCCAGGCCTTGTGGCTGCCTGCCACCATCCCAACCTTCACCCAGTGGCTC TACTCATCTGGAGGTGACCAAGCAGCCAACCAATCGGGTCCCCTGGAGGTCCTCAAATGCCT CCATATGGGCAACTGAGCACATCCTGCCACTCCCACCTCGTGCCTCAGAATGGACACCAGGC TCAGACAAGTGGAAAAGGTGAGAGAGGAGAGCAGGGCGCAGAGCCCCGTGGAGGCTGAGTTT GAGTCGTASCTGGAGCGAGGAAGAGCTTCAAGGTGTCCTTCGTGGAAACCTGCTGCGGGTCT GGCCGGTTCCCTCAGGGGCTGGAGGATGTGTCCACATACCCAGTCCTGATAGAGGAGTTGCT ACCACATCAGGGCAGTCATTGGATCTGAGTTCATCGGGATTGGTGGAAATTATGACGGGACT @TCCAT@GGGGTGCTGCAGTGCAACCTGCTTGCTAACGTGTCCACTGTGGCAGATCACTTTG TTGAATGTTCCCGATGATATCCTGCAGCTTCTGAAGAACGGTGGCATCGTGATGGTGACACT ACCTGACACTTACCTTCACCTGCAGTACACCATGGGCAGAGAGTTCCACCAAGTTCAGACAC TGGTCACTCACTGGACAGCAGCCTCTCTGTGCTGCGCAGTTTCTATGTGCTGGGGGGTGCGCT TCGCCCTGGAGCAGATTGACCTCATTCACCGCATGTGTGCCTCCTACTCTGAACTCGAGCTT GTTAACCTGCGAAATTTCAGCCATGGTCAGACCAGCCTGGACAGGCTTAGAGACACGGCCTCGT TGGACGGCCACAATGACCTGCCCCAGGTCCTGAGACAGCGTTACAAGAATGTGCTTCAGGAT AGCCTCTTCACCACGCCGGGTGTCCCCCAGCGCCCTCACTACCCCAGGCCTCACTACGCCAGG CCGTAACCCGCGCGGAGACCACGCCGGGCGCCCCAGAGCCCTCTCCACGCTGGGCTCCCCC GCTCAGCCGGCGGTATCTGCGGCGTCTGCTGCTGCTGCTACTGCTGCTGCTGCTGCGGCAGC CCAGGCTCCCGCGGCCGACCCCGCGCAAC<mark>AIG</mark>CAGCCCACGGGCCGCGAGGGTTCCCGGGC CGGGAGGCTGGGTCGTCATGATCCGGACCCCATTGTCGGCCTCTGCCCATCGCCTGCTCCTC

FIGURE 38

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59817
><subunit 1 of 1, 487 aa, 1 stop, 2 unknown
><MM: 53569.32, pI: 7.68, NX(S/T): 5</pre>

MOJTGREGSRALSRKYLRELLLILLILLIK, QPYTRAETTFGAPRALSTLGSPSIETTFGPVPS
ALTTFGLTFPGTFKTLDLRGRAQALMRSFFILVDEHNDLPQVLGRYKNVLQDVNIENFSHGQ
TSLLDRLADGLVGAQFYGSAVSCQSSQDOTAVRLALEQIDLIHAVCASYSELELVTSAEGINSS
QKLACLIGVXGGHSLDSSLSVLRSFYVLGVRYLTLTFTCSTFWAESSTKFRHHMTINVSGLT
SFCEKVVEELNRLGMNIDLSYABOTLIRVLEVSQAFVIFSHSAARAVCDNLLAVPDDILQL
SKOGGIVMVTLSMGVLQCNLLANVSTVADHFDHIRAVIGSSFIGIGROYDGTGRFPQGLSTSCH
STYPVLIEELLSRXWGLEQCULRANUTLAVFRQVEKVREESRAQSFVEAFFYGQLSTSCH
SHLVPQNGHQATHLEVTKQFTNRVFWRSSNASFYLVFGLVAAATLFTFTQWLC

Important features of the protein:

Signal peptide:

amino acide 1-36

Transmembrane domain:

amino acide 313-331

N-glycosylation sites.

amino acids 119-122, 184-187, 243-246 and 333-336

N-myristoylation sites.

amino acids 41-46, 59-64, 73-78, 133-138, 182-187, 194-199, 324-329, 354-359, 357-362, 394-399, 427-432 and 472-477.

Prokaryotic membrane lipoprotein lipid attachment site

amino acids 136-146

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FIGURE 39

CACCACAGCCCCTGTACTTGGGTTGCCTCTTGTCCCTGAACTTCGTTGTACCAGTGCATGGA GAGTTCTGAAGATATCCGGTGCAAATGCATCTGTCCACCTTATAGAAACATCAGTGGGCACA GAGAAAATTTTGTCCTCTTGTCTTAGAGTTGTGTGTAAATCAAGGAAGCCATCATTAAATTG CACAGTCACTGAGCCAGACGGTCGGTTGGAACATGAGACTCGAGGCTGAGCGTGGATCTGAA CTGCTGCCGGTCCCCTCACCTGCACTTGAGGGGTCTGGGCAGTCCCTCCTCTCCCCAGTGTC AGCTGGTGTTCGCTGTCCCCTGTGCACTTCTCGCACTGGGGCATGGAGTGCCCATGCATACT AGGACAGCTCTGATGGGAGAGCTGGGCCCCCTGAGCCCACTGGGTCTTCAGGGTGCACTGGA GTTCTTATCACCACCTCCCTCCCAGCCCCGGCCCTCAGCCCCAGCCCCAGCTCCAGCCCTG GGAACTCAGTGTCTGGGAGGAAAGCATGGCCCAGCATTCAGCATGTGTTCCTTTCTGCAGTG CCGCCTTCCAGCTCTGAGTCTTGGGAATGTTGTTACCCTTGGAAGATAAAGCTGGGTCTTCA ATGGAGACATTCGAGGCGGCCTCAGGAGTGGATGCGATCTGTCTCTCCTGGCTCCACTCTTG CTCCCTAACTTTAGAAATGTTGTACTTGGCTATTTTGATTAGGGAAGAGGGGATGTGGTCTCT CTACTTCTCCCTTCCCTCGGTTCCAGTCTTCCCTTTAAAAGCCTGTGGCATTTTTCCTCCTT TGTGGTTGGGTCAAGGCCCCAACACCATGGCTGCCAGGCTTCCAGGCTGGACAAAGCAGGGGG AGGTGCAGGAGCAGCGGAAGACAGTCTTCGATCGGCACAAGATGCTCAGC<u>TAG</u>ATGGGCTGG GGGACCCCGAGCAAACACAGTCCTGGAGCGTGTGGAAGGTGCCCAGCAGCGGTGGAAGCTGC CTGCACAATGAGGAGGAGAATGAGGATGCTCGCTCTATGGCAGCAGCTGCTGCATCCCTCGG ACATGGCCTTCCTGATGCTGGTGGACCCTCTGATCCGAAAGCCGGATGCATACACTGAGCAA CACCACCACCATCAAGGTCATCATTGTCÄTCTACCTGTCCGTGGTGGGTGCCCTGTTGCTCT GTGCCTGGCCATGACGTGGAGGCCTACTGCCTGCTGTGCGAGTGCAGGTACGAGGAGCGCAG AAGCTCTTATCTTTGGTGGCTGTGGTCGGGTGTTTGCTGGTGCCCCCAGCTGAAGCCAACAA TCCCTCTATGACTGCAATGTGAGGTGTCCGGCTTTGCTGGCCCAGCAAGCCTGATAAGC<u>ATG</u> TGCTAGGCTCTGTCCCACAATGCACCCGAGAGCAGGAGCTGAAAGCCTCTAACACCCACAGA

FIGURE 40

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA60278

<subunit 1 of 1, 183 aa, 1 stop</pre>

<MW: 20574, pI: 6.60, NX(S/T): 3

MKILISLVAVVGCLLVPPAEANKSSEDIRCKCICP?YRNISGHIYNQNVSQKDCNCLHVVEPM PVPGHDVEAYCLLCECRYEERSTTIKVIIVIYLSVVGALLLYMAPLMLVDPLIRKPDAYTE QLHNEEENEDARSMAAAASLGGPRANTVLERVBGAQQRWKLQVQEQRKTVFDRHKMLS

Important features:

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 90-112

N-glycosylation sites.

amino acids 21-24, 38-41 and 47-50

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FIGURE 41

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FIGURE 42

MAALMRSKDSSCCLLLLAAVLMVESSQIGSSRAKLNSIKSSLGGETPGQAANRSAGMYQGLA FGGSKKGKNLGQAYPCSSDRECEVGRYCHSPHQGSSACMVCRRKKKRCHRDGMCCPSTRCNN GICIPVTESILTPHIPALDGTRHRDRNHGHYSNHDLGWQNLGRPHTKMSHIKGHEGDPCLRS SDCIEGFCCARHFWTKICKPVLHQGEVCTKQRKKGSHGLEIFQRCDCAKGLSCKVWKDATYS SKARLHVCQKI

Signal peptide: amino acids 1-25

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FIGURE 43

CAGTCTGACAAGCTCATCACTGAATTCTGCTAGTCCAGTAGCAATGTCTTCCTCTTATGACC ATCCCAGCTTCTGCAGTGGAAATGCCTGGTTCAGCAGATGTCACAGGATTAAATGTGCAGTT TCCACCAGCCACAGCCCAAACACATCAAACTTGCTAAGCGGCGGATACCCCCAGCTTCTAAG CCTGGTTTGGAGTCCTTTCCCTTCCCAGGCAAAACTTCGAGAATCAACACCTGGAGACAGTCC CAGTTCTTAGCCAGTTGAGCCAGCGACAACAGCACCAGGCCAGGCAGTCACTGTTCCTCCT CCAAGTACACAGCAGAATAGTACAAGTCACCCTACAACTACTACTTCTTGGGACCTCAAGCC CTACTTGGGAGGCTGAGGCACAAGAATCGCTTGAGCCAGCTTGGGCTACAAAGTGAGACTCC TTTAAAGATGCTTGGGCCAGGCGGGGTGGCTGATGCCCATAATCCCAGTGCTTTGGGGGGGC GGTGGTCTCATAFTCTTCTGCCCTAATCAGACTGCACCACAAGTGCAGCATACAGTATGCAT TTTTGGACCAGGTGTTGGCTGTGGTGTTATTAGAAATGTCTTAACCACAGCAAGAAGGAGGT TGTGGAAAACACCAGTTGGTCAATGGCTCATTCGT<u>TAA</u>AAAGCAGCCCTTTTGCTTTTTTGT CAGCAAGCTACTCTTGTCATGGCTGGTGCCAACCAAACAGAGGAAGAGGATAGCTCACGTGA AGAGTT CTGTGCATAACAGGATCCCATACCAAAGCCCTGTGAGTTCATCAGAGTCAGCTCCA CTCCACTGTGAACAAGCTTTTGCAGCTTCCCCAGCACGACCATTGAAAATATCTCTGTGTCTG CCCAACATCCCAGTCCTCAGTCCTCAGTCATCTTGACTTCAAATCTCAACCTGAGCCATCCC TCACCAGCTCCCAGATTTTGGACCAGTTGAAAGCTCCGAGTTTGGGCCAGTTTACCACCACC GTCTGAAAAGA AAGGCAGGCAGATTGCCCAAGCTCAGGAGTTTGAGACCACCCTGGGCAACATGGTGAAACTC TCTTTATCAATGACCAGTGCAGTACAGAACTCCACATATACAACTTCCGTCATTACCTCCTG AAAATAGTAATCAGATTCCCATCAGCTTGTATTCGAAGTCTTTAAGTGAGCCTTTGAATACA TGGGGCTCTGGAATTTGGGTCAGAACCTTCTCTCTCTGAATTTGGATCAGCTCCAAGCAGTG TTTAAAGTCATCCGTCCTTGGCTCAGGATTTGGAGAGCTTGCACCACCAAAAAATGGCAAACA <u>ATG</u>TGTTTTAAAGCCTTGGGCAGAAATTCTGTATTGTTGAGGATTTGTTCTTTTATCCCCCT ttatattttagtaattcatatgttttagattataggttttaacatacttgtgaaaatacitg TAGCTGCATTTATTTAGTCAGTTTTCATTGCATAGTAATATTTTCATGTAGTATTTTCTAAG GTGTTGGGATTACAGGCGTGAGCCACCGCGCCCGGCCAACATCACGTTTTTAAAAATTGATT

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FIGURE 44

MCFKALGRNSVILRICSFIPLLKSSVLGSGFGELAPPKMANITSSQILDQLKAPSLGQFTTT
PSTQQNSTSHPTTTTSWDLKPPTSQSSVLSHLDFKSQPEPSPVLSQLSQRQQHQSQAVTVPP
PGLESFPSQAKLRESTPGDSPSTVNKLLQLPSTTIENISVSVHQPQPKHIKLAKRRIPPASK
IPASAVENPGSADVTGLNVQFGALEFGSEPSLSEFGSAPSSENSNQIPISLYSKSLSEPLNT
SLSMTSAVQNSTYTTSVITSCSLTSSSLNSASPVAMSSSYDQSSVHNRIPYQSPVSSSESAP
GTIMNGHGGGRSQQTLDSKYSSKLLLSMLVPTKQRKRIAHVMMKTPVGQMLIR

Signal peptide: amino acids 1-24

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FIGURE 45

CGGGCCCCTTTTTCTGCGCGACCGCGTGGCTGTGGGCGCGGATGCCTTTGAGCGCGGTGACT
TCTCACTGCGTATCGAGCCGCCTGGAGGTCGCCGACGACGACGGCACCTACTCCTCCTGCCACCTGCAC
CACCATTACTGTGGCCTGCACGAACGCCGCGTCTTCCACCTGACGGTCGCCGAACCCCACGC GGTGCTGGCGGTGGCGCGCGCGCACCCGCGCTTCTGACCTGCGTGAACCGGCGGGCACGTGT CAGGGGAGGGAGTGAAGTTGGTTTTGGGGTGGCCTGTGTTGCCACTCTCAGCACCCCACATTT GGACTCTGCCTGGGCTGGAGTCTAGGGCTGGGGCTACATTTGGCTTCTGTACTGGCTGAGGA CTTTGGGCCACCTGGGGCTGCACCCCTGCCCTTTCTCTGCCCCATCCCTACCCTAGCCTTG GCACCATCTGTTCTCCCCAGGGACCTGCTGACTTGAATGCCAGCCCTTGCTCCTCTGTGTTG CCTCCTGGGGTGCTGCCTGCCACCAAGAGCTCCCCCACCTGTACCACCATGTGGGACTCCAG GGACACTCCCATCAGAACTTGGCAGCCTTGAAGTTGGGGTCAGCCTCGGCAGGAGTCCCACT GGGCAGGAGTCCCACTCCTCCAGGGCTCTGCTCGTCCGGGGGCTGGGAGATGTTCCTGGAGGA aaaateccactgatgeccateatgeccteagaccettgggetetggeetgggggeetg aagacattectggaggacacteccateagaacetggeageeecaaaactggggteageetca AGCATAGCCCCCCCCCTGCGGCCTTTGCTCACGGGTGGCCCTGCCCACCCCTGGCACAACC GGAATTTGGCCTGGGCGTATGCAGAGGCCGCCTCCACACCCCTCCCCAGGGGGCTTGGTGGC CTCGGGGCATCTCCTGATGCTCCGGGGCTCACCCCCTTCCAGCGGCTGGTCCCGCTTTCCT GGCCCACAGCCCCCTGCCTGCCAAGTACATCGACCTAGACAAAGGGTTCCGGAAGGAGAACT TA CAGGAGTGAGGA CAT CCAGCTAGATTA CAAAAACAA CAT CCTGAAGGAGAGGGCGGAGCT AGTCAAAGGGGAAGGATGTTAACTTGGCGGAGTTCGCTGTGGCTGCAGGGGGACCAGATGCTT TGTCCTCCTGGCCGCCCGCAGGCGCCGCGGAGGCTACGAATACTCGGACCAGAAGTCGGGAA TTCTTCCAGCAGCTGGGCTACGTGCTGGCCACGCTGCTGCTCTTCATCCTGCTACTGGTCAC ACCCCACACTGGCGCGCGGCCACAACGTCATCAATGTCATCGTCCCCGAGAGCCGAGCCCAC GGAGCCGCCCCCCCGGGGCTCTCCGGGCAACGGCTCCAGCCACAGCGGCGCGCCCCAGGCCCAG GGACCGACCGGCACGTGGAGGAGGCTCAACAGGTGGTGCACTGGGACCGGCAGCCCCCGGC ACGCGGGGCTGTACACCTGCAACCTGCACCATCACTACTGCCACCTCTACGAGAGCCTGGCC TTGGAAACTTGTGCTTCTGCAGAGCTCTGCTGTTCTCCTGCACTCAGCGGTGGAGGAGACGC GCCGAGTGGGACAAAGCCTGGGGCTGGGCGGGGGGCC<u>ATG</u>GCGCTGCCATCCCGAATCCTGCT

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FIGURE 46

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA60618
<subunit 1 of 1, 341 aa, 1 stop
<MM: 38070, pI: 6.88, NX(S/T): 1</pre>

MALPSRILLMKLVLLQSSAVLLHSAVEETDAGLYTCNLHHHYCHLYESIAVRLEVTDGPPAT
PAXWDGEKEVLAVARGAPALLTCVNRGHVWTDRHVEBAQQVVHWDRQPPGVPHDRADRLLDL
YASGERRAYGPLFLRDRVAVGADAFERGDFSLRIEPLEVADEGTYSCHLHHHYCGLHERRVF
HLTVAEPHAEPPRGSPGNGSSHSGAPGPDFTLARGHNVINVIVPESRAHFFQQLGYVLATL
LLFILLLVTVLLAARRRGGYEYSDQKSGKSKGKDVNLAEFAVAAGDQMLYRSEDIQLDYKN
NILKERAELAHSPLPAKYIDLDKGFRKENCK

Important features: Signal peptide: amino acids 1-19

Transmembrane domain: amino acids 237-262

N-glycosylation site. amino acids 205-208

Cell attachment sequence.
amino acids 151-154

Coproporphyrinogen III oxidase proteins. amino acids 115-140

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FIGURE 47

GGTGGACACTTCCTCCTGGACCCGTGGTTTTTTTTGCGGTCACCATTGTCTGCATGGTGATCC GGACCCTGAGGGCTCAGACATCCTGAACTACTTTGAGAGCTACCTTGCCGTTGCCTCCACCG GTGGCACATACATCATCTTCTTCAGCCTGGGCATTGGCAGTCTACTGCCATGGAACTTCTTT ACTGCTTGAGAAGCTGCTGGACCGCCCGCCCCCTGGCCTGCAGAGGCCCCGAGGACCGCTTCT CTTCAGAGCCTTTGAAGATGAGAAGAGAGTGCAGGAGGGCTGGGGGGCCATGGAGGAAAGGCC $\mathtt{CTCAGCCTGCTCTACCCTCCTGGTGCACCTCATC}_{\mathtt{TAG}}\mathtt{AAGGGAGGACACAAGGACATTGGTG}$ @AGCTGGCTGAGGCCACGGGAGTGGTGATGTCCTTTTATGTGTGCTTGGGCTTAACACTGGG GGCTCAGCAACGGCTACCTCAGCACCCTGGCCCTCCTCTACGGGCCTAAGATTGTGCCCAGG GTGGCCGGCAGCTCACCGCCTGGATCCAGGTGCCAGGGGCCCAACAGCAAGGCGCTCCCAGG GTGGACCACCAAGTTTTTCATCCCCCTCACTACCTTCCTCCTGTACAACTTTGCTGACCTAT GCCCCATCCTGAAGAAGACGGCCAGCCTGGGCTTCTGTGTCACCTACGTCTTCTTCATCACC GGACTCCCTCAGTGCCCCTTCGGTGGCCTCCAGATTCATTGATTCCCACACACCCCCTCTCC AGGTACTACATGAGGCCTGTTCTTGCGGCCCATGTGTTTTCTGGTGAAGAGGAGCTTCCCCA OCACCATCTTCCTCGTGCTCTGCATGGGACTCTACCTGCTGCTGTCCAGGCTGGAGTATGCC ATTGGTGGACTTGGCTGCATCCAGTGATGTGAGGAACAGCGCCCTGGCCTTCTTCCTGACGG AGGAACTCCCAAGCACTGATATCAGGAGGAGCCATGGGCGGGACGGTCAGCGCCGTGGCCTC CGTGTCCTGGCCTCACTGACGGTCATCCTGGCCATCTTCATGGTGATAACTGCACTGGTGAA TGCCCTCCATGCTGTGCCTGGTGGCCAACTTCCTGCTTGTCAACAGGGTTGCAGTCCACATC CAGCACAGTTCAAACTCCACCTACGGAACCACAAGCAGCAGTCTCCGAGCTGACCAGGAGGC CGCCGGAGGCAGCGGCGCGCGCGCAGCGGCGAC<u>ATG</u>GCCGTTGTCTCAGAGGACGACTTT TTTTCAAAAAAAGAGGGATCCTCATGACCTGGTGGTCTATGGCCTGGGTCAAGATGAGGGTC GCTTCATTCCAGAGGGACCAGAGGGCCTCCCTGTGCAAGGGATCAAGCATGTCTGGCCTGGG GCGGGTGAACAACTGCCCACTAACCAGACTGGAAAACCCCAGAAAGATGGGCCTTCCATGAAT AGTCCCCTGGCATGGTCAGTCCTCAGGCCCAAGACTCAAGTGTGCACAGACCCCTGTGTTCT gacagegagatgcaagcaaatgeteageteteettaceetgaaggggteteeetggaatgga NAGCCAGTGCCANAAACCCAGCCATGGGCTCTTTGCAACCTCCCAGCTGCGCTCATTCCAGCT ^ACATTCCACCTTCTTCTAGCCCTTCAAAGATGCTGCCAGTGTTCGCCCTAGAGTTATTACA CCTGAGACAGTTGAAGAAGAAATAGCACAAATCAGGGGTACTCCCTTCACAGCTGATGGTTA CCACCTGAAGACTGTGGTCTTCCAGTCCGATGTGTACCCCGCACTCCTCAGCTCCCTGCTGG TICGTGCTCCTCCGGACCTGCCTCATCCCCCTCTTCGTGCTCTGTAACTACCAGCCCCGCGT AGCCTCATCTACCCCGCCGTCTGCACCAACATCGAGTCCCTCAACAAGGGCTCGGGCTCACT TCAGCGGTGCCTCCACTGTCTTCAGCAGCAGCATCTACGGCATGACCGGCTCCTTTCCTATG

FIGURE 48

MAVVSEDDFQHSSNSTYGTTSSSLRADQEALLEKLLDRPPPGLQRPEDRFCGTYIIFFSLGI
GSLLPWNFFITAKEYMMFKLRNSSSPATGEDPEGSDILNYFESYLAVASTVPSMLCLVANFI
LVNRVAVHIRVLASLTVILAIFMVITALVKVDTSSWTRGFFAVTIVCMVILSGASTVFSSSI
YGMTGSFPMRNSQALISGGAMGGTVSAVASLVDLAASSDVRNSALAFFLTATIFLVLCMGLY
LLLSRLEYARYYMRPVLAAHVFSGBEELPQDSLSAPSVASRFIDSHTPPLRPILKKTASLGF
CVTYVFFITSLIYPAVCTNIESLNKGSGSLWTTKFFIPLTFLLYNFALLCGRQLTAWIQVP
GENSKALPGFVLLRTCLIPLFVLCNYQPRVHLKTVVFQSDVYPALLSSLLGLSNGYLSTLAL
LYGPKIVPRELAEATGVVMSFYVCLGLTLGSACSTLLVHLI

Transmembrane domain:

amino acids 50-74 (type II), 105-127, 135-153, 163-183, 228-252, 305-330, 448-472

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FIGURE 49

GCACATTGAAGGCGGCCACTCAAACACCGATCGCCCGTCGCGCATGATTTTCTACCCGCCGC CTGCACTACGTGCCGGCCACCAAGGTGTTCCTAAGCTTCCGCAGGCCCTTCTGGCGCGAGGA CGGCCGGCCGTGCAGCTTCTGGGAGACGTGATGTCCGAGGATGGCTTCTTCTATCTCAGCTT <mark>ቚቚቚቚቚቚቚቚቚቚቚቚቚቚቚፙፙፙፙፙፙፙፙፙፙፙፙፙፙፙፙፙፙፙፙፙ</mark> CCAGTTATCTCTCCAAAACACGACCCACACGAGGACCTCGCAT<u>TAA</u>AGTATTTTCGGAAAAA GTGGCCAGCAGCCCCTCGCATGACCTGGCAAAGGAAGAAGGCAGCCACCCTCCAGTCCAAGG CGGACACGGCCAGCCCCGAGGGGCACGCATCTGACATGGAGGGGCAGGGGCATGTGCATGGG GACGGCGGTCAAGTCGGCGCTGCGCGCCGCCATCAAGATCAACAGCCGGAAGGGGCCTGCAI GTCCCTTANGGCCGCATCTACTTNGCCGGCGAGCACACCGCCTACCCGCACGGCTGGGTGGA ©CCAGGGTGGCTTTGTGGTACAGCCGCCGCGGGGTCTCTGGCAAAACCGAAAAAGGATGACTGGACG TGTCGTGCGCCAGCTCTGGGACGGCACCGGCGTCGTCAAGCGTTGGGCGGAGGACCAGCACA GGCTTGAGCCGGGAAGAGGCGTTGCGCTTGGCGCTCGACGACGTGGCGGCATTGCACGGGCC CGCGCGAGGGCGCGCTGCTGGCCTCGTACACGTGGTCGGACGCGGCGGCAGCGTTCGCC CCCGGCGCGAATCTGAAGGTGCTGAAGGCCGACGTGGTGCTGACGGCGAGCGGACCGG GCGCCCGTGGTGGCGATGACCCAGGGACCGCACGATGTGCACGTGCAGATCGAGACCTCTCC GTGGCTGGGACCTGCTGCCGCGCGCGCGCTGCTGAGCTCGCTGTCCGGGCTTGTGCTGTTGAAC CGCCGAGGCCCTCCGGGCCCACAGCTGCCTCAGCGACAGACTCCAGTACAGCCGCATCGTGG CGATGAAGAAGTTTGAAAGGCACACGCTCTTGGAATATCTTCTCGGGGAGGGGAACCTGAGC CATCTACCAGATGGCTCTCAACCAGGCCCTCAAAGACCTCAAGGCACTGGGCTGCAGAAAGG AAGGTGCCCGAGAAGCTGGGCTACGCCTTGCGTCCCCAGGAAAAGGGGCCACTCGCCCGAAGA agtacgacaagaacacgtggacggaggtgcacgaagtgaagctgcgcaactatgtggggag CTCTCACAGGATCCTCCACAAGCTCTGCCAGGGCCTGGGGCTCAACCTGACCAAGTTCACCC TTCACCTACCGGGACCAGAACACGGGCTGGATTGGGGAGCTGGGAGCCATGCGCATGCCCAG TCAGCGATGCTGGACACAAGGTCACCATCCTGGAGGCAGATAACAGGATCGGGGCCGCATC GAAGCCCCAGAGGGTGATTGTGGTTGGCGCTGGTGTGGCCGGGCTGGTGGCCGCCAAGGTGC ATGCAGGATCCTGACTATGAGCAGCTGCTCAAGGTGGTGACCTGGGGGCTCAATCGGACCCT TCAGCCTGGTGGCCTCCCAGGACTGGAAGGCTGAACGCAGCCAAGACCCCTTCGAGAAATGC TCTCCCACCGAGAGTC<u>ATG</u>GCCCCATTGGCCCTGCACCTCCTCGTCCTCGTCCCCATCCTCC GACAGT GGAGGGCAGTGGAGAGGACCGCGCTGTCCTGCTGTCACCAAGAGCTGGAGACACCA

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FIGURE 50

MAPLALHLLVLVP ILLGLVASQDWKAERSQDPFEKCMQDPDYEQLLKVVTWGLNRTLK?QRV
IVVGAGVAGLVAAKVLSDAGHKVT ILEADNR I GGR I FTYRDQNTGW I GELGAMRWPSSHR IL
HKLCQGLGLNLTKFTQYDKNTWTEVHEVKLRNYVVEKVPEKLGYALRPQEXGHSPEDIYQWA
LNQALKDLKALGCRKAMKKFERHTLLEYLLGEGNLSRPAVQLLGDVMSEDGFFYLSFAEALR
AHSCLSDRLQYSR I VGGWDLLPRALLSSLSGLVLLNAPVVAMTQGPHDVHVQIETSPPARNL
KVLKADVVLLTASGPAVKR I TFSPPLPRHWQEALRRLHYVPATKVFLSFRRPFWREEHIEGG
HSNTDRPSRM I FYPPPREGALLLASYTWSDAAAPAGLSREEALRLADDVAALHGPVVRQI
MDGTGVVKRWAEDQHSQGGFVVQPPALMQTEKDDWTVPYGR I YFAGEHTAYPHGWVETAVKS
ALRAAI KINSRKGPASDTAS PEGHASDMEGQGHVHGVASSPSHDLAKEEGSHPPVQGQLSIQ
NTTHTRTSH

Signal peptide: amino acids 1-21

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FIGURE 51

FIGURE 52

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA60775</pre>

<subunit 1 of 1, 739 aa, 1 stop
<hww: 82263, pI: 7.55, NX(S/T): 3</pre>

MDALKPPCLMRNHERGKKDRDSCGRKNSEPGSPHSLEALRDAAPSQGLNFLLLFTKMLFIFN
FLFGBLPTBALICILTFGAAIFLWLITR QPVLFHLLDLNNQSVGIEGGARKGVSQKNNDLTS
CCFSDAKTMYEVFQRGLAVSDNGPCLGYRKPNQPYRWLSYKQVSDRAEYLGSCLLHKGYKSS
PDOFVGIFAQNRPEWIISELACYTYSMVAVPLYDTLGPEAIVHIVNKADIAMVICDTPQKAL
VLIGNVEKGFTPSLKVIILMDFFDDDLKQRGEKSGIEILSLYDAENLGKEHFRKPVPPSPED
LSVICFTSGTTGDPRGAMITHQNIVSNAAAFLKCVEHAYEPTPDDVAISYLPLAHMFERIVQ
AVVYSCGARVGFFQGDIRLLAADDMKTLKPTLFPAVPRLLNRIYDKVQNEAKTPLKKFLLKLA
VSSKFXELQKGIIRHDSFMDKLIFAKIQDSLGGRVRVIVTGAAPMSTSVMTFFRAAMGCQVY
EAYGQTECTGGCTFTLPGDMTSGHVGVPLACNYVKLEDVADMNYFTVNNEGEVCIKGTNVFK
GYLKDPEKTQEALDSDGWLHTGDIGRWLPNGTLKIIVKKRLACQGEYTAPEKIENIYNR
SQPVLQIFVHGESLRSSLVGVVVPDTDVLPSFAAKLGVKGSFEELCQNQVVREAILEDLQKI
GKESGLKTFEQVKAIFLHPEPFSIENGLLTPTLKAKRGELSKYFRTQIDSLYEHIQD

Important features:

Type II transmembrane domain:

amino acids 61-80

Putative AMP-binding domain signature.

amino acids 314-325

N-glycosylation site.

amino acids 102-105, 588-591 and 619-622

52/270

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FIGURE 53

GAAGAAAGAAGCTTATGAAGTGGAAGTTCACAGGCTGCTCAGTGAGGCTGAGGTTCTGGACC GTTCAGCCCTGACCCACTCCCAGACAACAAGGTCCTCAATGTGCCTGTGGCTGTCATTGCAG TTCTGCAGCAAAGTTGAGGGCTATGGAAGTGTATGCAGCTGCAAGGACCCCACACCCATCGA GCTCAGCAGAAGAGGCAGAGTGCCACTGGGCAGACACAGAGCTGAACCGTCGCCGGCGGGGG GACACTGGACCAGGCCTCCTCAGCCTTCTCTTTGTCCAGATTTCCAAAGCTGGATAAGTT TTTATTCGAATGGAGAAAGATGATGACTTCACCACCTGGACCCAGCTTGCCAAGTGCCTCCA
TATCTGGGACCTGGAATGTGCGTGGCAACCATCGGGGCCTGTGGAGATTGTTTCGGAAGAAGA ACAGCAAGAACCCTTGTGAAGACTCTTTCCTGCCAGACACAGAGGGGCCACACCTACGTGGCC TTTCCCGATCCTACCACTTTGGCATCGTCGGCCTCAACATGAATGGCTACTTTCACGAGGCC TTGGGACATGTGGATGCGGATGCCTGAACAACGCCGGGGCCGAGAGTGCATCATCCCTGACG CGGCTGAGGACCCAGCACTACTGTACCGTGTGGAGACCATGCCTGGGCTGGGCTGGGTGCTC GTTTGGTCTGAGGGGCATCCAGCATACTCCCATCAGCATCAAGAATGCCCGCGTGTCTCAGC TAAGTCACCTGCCCTCTCTTCCTGGGGGGACCCAGTCCTGCTGAAGACAGATGTGCCATTGA CAACATGGTAGCGCCCGGCCGAGTGCTCATCTGCACTGTCAAGGATGAGGGCTCCTTCCACC AGGCCCGGGAGCAGGGCCGGGGCATCCATGTCATTGTCCTCAACCAGGCCACGGGCCACGTG GGTGTATTCAAGTCGCAGCAAAGTATATGTGGCAGTGGATGGCACCACGGTGCTGGAGGATG CTAGGCCCCCTGGAGCCCCCACGGCGCAGAGGCAGTGGTCCCCGGCGGGTCCTGGACGTAGA CTCGGCGAGCCATCAGTGAAGCCAATGAAGACCCAGAGCCAGAGCAAGACTATGATGAGGCC GACAGGGGCCGTGCTTTTCCTGCTGGTGACTGTCATTGTCAATATCAAGTTGATCCTGGACA CCGGT<u>ATG</u>GACGACTGGAAGCCCAGCCCCCTCATCAAGCCCTTTGGGGCCTCGGAAGAAGCGG TTTTTGGGCTGGAATGCTGCCCTGAGGGTGGGGCTGGCTCTTACTCAGGAAACTGCTGTGCC acctatttattgactgtcctgagggccttgaaaacaggccgaacctggagggcctggatttc ATCCCTAGCAGCTCATCCTGCCCTTTGAATACCCTCACTTTCCAGGCCTGGCTCAGAATCTA aaaagtctatttatttacttccttgttggagaaggcaggagagtacctgggaatcattacg TGAGACTTAATTACTAACTCCAAGGGGAGGGTTCCCCTGCTCCAACACCCCGTTCCTGAGTT ACCACTTCCTGGTGGGGGGTCCCGGCTTCCCCCTACTCAGTGAAGAAGCCACCCTCAGTC TACTTCAAGAAGCACAAGTTCAACACGGTTCCAGGTGTCCAGCTCAGGAATGTGGACAGTCT aggaggtecttgtacaaggaggagettgageeeaagtggeetaeaeeggaaaaagetetggga ACTGGAGGAGGATGACAGCCTGTACTGCATCTCTGCCTGGAATGACCAGGGGTATGAACACA CCTCAGATGATAACAGTTTTCATTGACGGCTACTATGAGGAACCCATGGATGTGGTGGCACI TGGAGGGACACATGGGCCTTCGTGGGACGAAAAGGAGGTCCTGTCTTCGGGGAGAAAACATTC TCAAGGACACAGCCAAGGCTCTGCTGAGGAGCCTGGGCAGCCAGGCTGGCCCTGCCCTGGGC atggcaaaacgtgtgtttgacacgtactcacctcatgaggatgaggccatggtgctattcct AGCTGGTACCTTACCTGGAAGTATAAACTGACAAACCAGCGGGCCCTGCGGAGATTCTGTCA CCCGGGGCCCCTAAGCCATTCCTGAAGTCATGGGCTGGCCAGGACATTGGTGACCCGCCAAI GGAGGCGGAGGCCGCGGCGAGCCGAGCAGTGAGGGCCCTAGCGGGGCCCGAGCGGG ICCCTCCATCCTGTAGGATTTTGTAGATGCTGGTAGGGGCTGGGGGCTACCTTGTTTTTAACA actacaaggccagcctcactgccactttcaacctgtttccggaggccaagtttgctgtggtt

FIGURE 54

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA61185

><subunit 1 of 1, 660 aa, 1 stop

><MW: 75220, pI: 6.76, NX(S/T): 0

MDDWKPSPLIKPFGARKKRSWYLTWKYKLTNQRALLRFFCQTGAVLFLLVTVIVNIKLILDTR
RAISEANEDPEPEQDYDEALGRLEPPRRROSGPRRVLDVEVYSSRSKVZVAVDGTTVLEDEA
REQGRGIHVIVLNQATGHVMAKRVFDTYSPHEDEAMVLFLAMVAPGRVLLCTVKDEGSFHLK
DTAKALLRSLGSQAGPALGWRDTWAFVGRKGGPVFGEKHSKSPALSSWGDPVLLKTDVPLSS
AEBABCHWADTELNRRRRFCSKVEGYGSVCSCKDPTPIEFSPDFLPDNKVLMVPVAVIAGN
RPNYLYRMLRSLLSAQGVSPQMITVFIDGYYEEPMDVVALFGLRGIQHTPISIKNARVSQHY
KASLTATFNLFPEAKFAVVLEEDLDIAVDFFSFLSQSIHLLEEDDSLYCISAMNDQGYEHTA
EDPALLYRVETMPGLGWVLRRSLYKEELEPKWPTPEKLMDWDMWMRMPEQRRGRECIIPDVS
RSYHFGIVGLMMNGYFHEAYFKKHKFNTVPGVQLRNVDSLKKEAYEVEVHRLLSEAEVLDHS
KNPCEDSFLPDTEGHTYVAFIRMEKDDDFTTWTQLAKCLHIWDLDVRGNHRGLWRLFRKKHH
FLVVGVPASPYSVKKPPSVTPIFLEPPDKEEGAPGAPBQT

Important features of the protein:

Transmembrane domain:

amino acids 38-55

Homologous region to Mouse GNT1

amino acids 229-660

54/270

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FIGURE 55

CTTATCAGGACAACCACTTCTCGAACTGTAATAATGAGATAATAATATCTTTATTCTTTATCCCCTT CAAAGAAATTACCTTTGTGTCAAATGCCGCTTTTGTTGAGCCCTTAAAATACCACCTCCTCATGTGTAA ATTGACACAATCACTAATCTGGTAATTTAAACAATTGAGATAGCAAAAGTGTTTAACAGACTAGGATA GTTCTGTAATTAAGCTATGCTCTTTTCTTYAGTTTAAAGGCTGTGCTACTTTATCCATTGATTTTTAAAATGGTAGGTGAAGGCTGATAAGGTCATAAGGTCATAAGGTCATAAGGTCATAAGGTGATAAGGTGATAAAGGTGATAAAGGTGATAAAGGTGATAAAGGTGATAAAGGTGATAAAGGTGATAAAGGTGATTCTAGTTAATCTGGGATTAAGGTGAGAAAATGATAAGGGATTGAAAAGGTAAGGGATTTAAGAGGATTTTAAGAGGATTTTAAGAGGATTTAAGAGGATTTAAAAGGGATTTAAAAGGGATTTAAAAGGGATT GGTGACATACTTAGGACTGAGTAAGAGCGGTAAAGAAGCCCTTTCAGAGGTGGACGCCACGGGAGTGG CCATGCTTTTCTCTGCCGGGACATTTCTTTATGTTGCCACAGTACATGTCCTCCCTGAGGTGGGCGGA Gactggtgtgagacttgaggtttcatctagtccttcaaaactatatggttgcctagattctctctgge ATTTTACTACCAAGAGAAGGTATAGTATGGAAAGTCCAAATGACTTCCTTGATTGGATGTTAACAGCT attratitecticatgaattigteaciggateageagetgiggaaataaagetigigageeeteiget TATTAATTTATTTTTACTTTCTATACCATTTCAAAACACATTACACTAAGGGGGAACCAAGACTAGTT ATTTTTTTTCATATTTGCCAAAATTTTTGTAAACCCTGTCTTGTCAAATAAGTGTATAATATTGTAT GGTTCTGGGTTGGCTCATCCCTCTCATCCTGTCAGGACACCAGCAT<u>TAA</u>ATGTTCAAGGTCCAGC CTTGGTCCAGGGCCGTTTGCCATCCAGTGAGAACAGCCGGCACGTGACAGCTACTCACTTCCTCAGTC ggcttagagcggaatcgaatcagaaagcacttgctggtctttgcattggcagcagcaccagttatgtccat TGCTGCAGCTGATGGTGTTGCTTTGGGAGCAGCAGCATCTACTTCACAGACCAGTGTCCAGTTAATTG TITCCCTCGTTCTGGGCTTCGTTTTCATGTTGCTGGTGGACCAGATTGGTAACTCCCATGTGCATTCTACATCACAACACCACGCTGGGTCTGGTTGTCCA GTGCTGGCCTTCTCTGTGGAACTGCTCTGGCAGTCATCGTGCCTGAAGGAGTACATGCCCTTTATGAA CGTGGCCGGAATCATTCCCTTGGCTGTTAATTTCTCAGAGGAACGACTGAAGCTGGTGACTGTTTTGG AAGGAGGGCAGA<u>ATG</u>GATGATTTCATCTCCATTAGCCTGCTGTCTCTGGCTATGTTGGTGGGATGTTI CTGTTTAAAGAACCTAAGCACCATTTAAAGCCACTGGAAATTTGTTGTCTAGTGGTTGTGGGTGAATA CGGACGCGTGGGCTGGTGGGAAGGCCTAAAGAACTGGAAAGCCCACTCTCTTGGAACCACCACAC ICTTCAGGGCAGTGGACGTAGTTTGTAAAAACGTTTTCTATGACGCATAAGCTAGCATGCCTATG

EIGURE 56

MDDFISISLLSLAMLVGCYVAGIIPLAVNYSEERLKLVTVVLGAGLLCGTALAVIVPEGVHAL
YEDILEGKHHQASETHNVIASDKAAEKSVVHEHEHSHDHIQLHAYIGVSLVLGFVYMLLVDQ
IGNSHVHSTDDPEAARSSNSKITTTLGLVVHAAALDGVALGAAASTSQTSVQLIVFVAIMLHK
APAAFGLVSFLMHAGLERNRIRKHLLVFALAAPVNSMVTYLGLSKSSKEALSEVNATGVAML
FSAGTFLYVATVHVLPEVGGIGHSHKPDATGGRGLSRLEVAALVLGCLIPLILSVGHQH

Signal peptide:

amino acids 1-18

Transmembrane domain:

amino acids 37-56, 106-122, 211-230, 240-260, 288-304

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FIGURE 57

CACAACTTCCAGCTGGAGAGCGTCAACAAGCTGTACCAGGACGAAAAAGGCGGTTTTTGGTGAA GCAGCAGGCCTGCCACACACAGAGGTGCCACAAGGGAAAGGGAAACGTGCTTGGTAACAGCAA GTGAAAACAACGACCAGAGACAGCAGCTCCAAGCCCTCAGTGAGCCTCAGCCCAGGCTGCAG SGAATTACGGCAGGCTGCAGCAGGATGTCCTCCAGTTTCAGAAGAACCAGACCAACCTGGAG ATCGTCTTGGGCTTCAACTACTGGATTGCGAGCTCCCGGAGCGTGGACCTCCAGACACGGAT GAAACGGGCGTCGCAGCATGAAGTCGCCGCCCCTCGTGCTGGCCGCCCTGGTGGCCTGCATC CGAGTGGCGGCCGGAGCCTCGAAAAGAGATTCTCAGCGCTGATTTTGAG<u>ATG</u>ATGGGCTTGG TTTTTAATGTTGAAGATCAGAAAAGAGACACCATAAATTTACTTGATCAGCGTGAAAAGCGG TGAAGCAGAATCTGAGACAGACAAGCAAGCCCCTGGCAGGGAATGACAGAAACATAGATG GCCGGGGAAGGGAGAAACCAGCAGAAAACTGAGAGGAGAAGATGACTACAACATGGATGAAAA AGAACTGGGCCAGACCCCACAGGTGCAGGCTGCCCTGTCAGTGAGCCAGGAAAATCCAGAGA CCAGGCCGGGAGCAGGTGGTAGAAGACAGACCTGTAGGTGGAAGAGGCTTCGGGGGAGCCGG GTCCCAGACACCAGCCCCCAGTTCCGAAGTGGTTTTGGATTCAAAGAGACAAGTTGAGAAAG TGAGGAGCGAATAGAAGAGGTCACCAAAAAGGGGAATGAAGCTGTAGCTTCCAGAGACCTGA AGGAAGTTCTCCTACGACCTGAGCCAGTGCATCAATCAGATGAAGGAGGTGAAGGAACAGTG TAACATCACCACAGGTGAGAGGCTCATCCGAGTGCTGCAAGACCAGTTAAAGACCCTGCAGA AGAACGAGTTCCAGGGAGAGCTGGAGAAGCAGCGGGAGCAGCTTGACAAAATCCAGTCCAGC GCTCGAGGCCGGCGGCGGGGAGAGAGCCACCCGGGCGCCTCGTAGCGGGGCCCCGGATCCC aatcatacactc<u>tga</u>attgaactggaatcacatatttcacaacagggccgaagagatgacta tggagggccctgagcgagaccagcttgtcatccccgacggacaggaggaggagcaggaagca aggaaaccaatgagatccaggtggtgaatgaggagcctcagagggacaggctgccgcaggag

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FIGURE 58

MMGLGNGRRSMKSPPLVLAALVACIIVLGFNYWIASSRSVDLQTRIMELEGRVRRAAAERGA
VELKKNEFOGELEXQREQLDKIQSSHNFQLESVNKLYQDEKAVLVNNITTGERLIRVLQDQL
KTLQRNYGRLQQDVLQFQKNQTNLERKFSYDLSQCINQMKEVKBQCEERIEEVTKKGNEAVA
SRDLSENNDQRQQLQALSEPQPRLQAAGLPHTEVPQGRGNVLGNSKSQTPAPSSEVVLDSKR
QVEKEETNEIQVVNEEPQRRLPAGEPGREQVVEDRPVGGRGFGGAGELGQTPQVQAALSVSQ
ENPEM3GPERDQLVIPDGQEEEQEAAGEGRNQQKLRGEDDYNMDENEAESETDKQAALAGND
RNIDVFNVEDQKRDTINLLDQREKRNHTL

Signal peptide:

amino acids 1-29

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FIGURE 59

COMPRIGATIVES CONTRIBUTION CONTRIBUTION AND ADDRESS CONTRIBUTION AND ACCORDING THE CONTRIGORY CONTRIBUTION AND ACCORDING CONTRIBUTION ACCORDING CONTRIBUTION AND ACCORDING CONTRIBUTION ACCORDING CONTRIBUTION AND ACCORDING CONTRIBUTION ACCORDING CONTRIBUTION ACCORDING CONTRIBUTION AND ACCORDING CONTRIBUTION ACCORDING CON

FIGURE 60

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA62809

subunit 1 of 1, 1089 aa, 1 stop

<MW: 118699, pI: 8.49, NX(S/T): 2

AKKLSOMDQVIQGLVERLENDTLLVVAGDHGMTINGDHGGDSELEVSAALFLYSFTAVFPST
PPEEPFVIPOVSLVFTLALLIGLP1FFGNIGEVWAELFSGGEDSOPHSSALAQASALHINAQ
QVSREUHTVSAATODLQAKELHQLUNLFSKASADYOMLQSPKGABATLPTVIAELQGFLRG
ARAMCIESMARFSLVRMAGGTALLIAASCFICLLASQMALSPGFFFCPLLLTPVAWGLVGAIA
VAGLLGTIELKLDLVLLGAVAAVSSFLPFLWKANAGWSKRPLATLFPIPGFVLLLLLIFRLA
VFSDSFVVAEARATPF1LGSFILLLLVVQLHWEGQLLPFKLLTMPRLGTSATTNPPRHNGAY
AURLGIGLLLCTRLAGLFHRCPEETFVCHSSPMLSFLASMVGGRAKNLWYGACVAALVALLA
AVRABLGRYGNLFFLHGSFILLLVVQLHWEGTAXWYGGRAKNLWYGACVAALVALLA
AVRLMIRKYGNLKSEPFPHLFVCHSSPMLSFLASMVGGRAKNLWYGACVAALVALLA
AVRLMIRKYGNLKSEPPHLFVRWGLPLWALGTBAYWALASGADERPHLRULYGGSMVLP
RAVAGLAASGLALLLMKFVTVLVKAGAGAPKTRTVLTPFSGDFDSADLDYVVPQIYRHMGE
EFGRULERTKSQGPUTVAAYQLGSVYSAAWVTALTLLAFPLLLHHARRISLVFLLFLVSSFL
LLHLLAAGIPVTFGGPFTVPWQAVSAWALMATQTFFXSTGHDFVFPAIHWHAAFVGFFEEGHGS MASR FSR VVLVL I DALRFDF AQ PQHSHVPRE PPVSL PFLGKLSSLQR I LEIQPHHARLYRSQ VDP PTTTMQRLKALTTGSL PTF I DAGSNFASHA I VEDNL I KQLTSAGRR VVEMGDDTWKDL F PGAFSKAFFFF PSFNVRDLDTVDNG I LEHLYPTMDSGEMDVL I AHFLGVDHCGHKHGPHHPEM CTWLPALLVGANTFASHLLFAVGCPLLLLMPFLCESQGLRKRQQPPGNEADARVRPEEEESB LMEMRLRDAPQHFYAALLQLGLKYLF ILGIQILACALAASILRRHLMVWKVFAPKFIFEAVG MQKASVLLFLAWVCFLFYAGIALFTSGFLLTRLELTNHSSCQEPPGPGSLPWGSQGKPGACW fivssvglllgialvmrvdgavsswfrqlflaqqr

Important features:

Signal peptide:

amino acids 1-16

Transmembrane domains:

amino acids 317-341, 451-470, 481-500, 510-527, 538-555, 831-850, 1016-1034, 1052-1070

Leucine zipper pattern.

amino acids 843-864

N-glycosylation sites.

amino acids 37-40, 268-271

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FIGURE 61

CAAACGTTACAGTACTCATACACCCCTCAGCTCCAAGACTTAGACCCCCTGGCGCAGGAGCA TGTTCTATGCAGAGAAAGCAGTCAATAAATGTTTGCCAGACTGGGTGCAGAATTTATTCAGG GTTCATGCATGTAGGTCTCTTAACAATGATGGTGGGCCTCTGGAGTCCAGGGGCTGGCCGGT TIGTCAGIGICIGIGAGAAITACIIAIIITCIITICCCTATTCTCATAGCACGIGIGIGAITG AAGTGAGTCACCCCTTTGATCCCAGCCATAAAGTACCTGGGATGAAAGAAGTTTTTTCCAGT TATATGTGCAGATGGAAAAC<u>TGA</u>TGCCAACACTTCCTTTTGCCTTTTGTTTTCCTGTGCAAAC TCCAGACAGGCCACCAGGAGAAAATGAAACCTATCTCATGCAATTCATGGAGGAATGGGGGT AAACTGGCAGGCTGTGTATTCCTTCGCTGTCCAGCTTCGACCAGGATTCAGAGGGCTGCGAG CACAGACTCGGAGGAGGGGCCGGAGGAAGAGCCATCGACGACCCTGGTCGACTGGGATCCCC ATATGATGTCAGAACCACTGACATTTGTGCGGGGCCTGAAGAGCAGGAGCTCAGTTTGCAGG CTCACCCAGCAAGAGTCCCTCAGCAGAACAATACCCCCGGATAAAACAGTCATTGAATATGA GGTATGCTTCGCATTTGATGGAAATTTTTTTGTGACTCTGAAGAAAACACGGAAGGTACTTCT TGATCCTCAGCCCAGCGGGAACCTGAGGCCCCCTCAGGAGGAAGAGGAGGTGAAACATTTAG TCTAAAATTTCTCATCAGGATATGAGTTTACTGGGAAAAAGCAGTGATGTATCCAGCCTTAA GATTCTTTGTGCCTGCTGAAAAATCGTGATTAACTTTATCACCCTCAATATCTCGGATGAT CGTTGGCAAAGAGAAACACCCAGCAAATTTGATTTTGATTTATGGAAATGAATTTGACAAAA CCCATATCTATTACCOTGTTTCTTTTTTCTGTGATGGGCTATTCCATCTACCGATATATCCA CCAGGACTTTGAAAAGATCAATCATCAGAGTTCAAGGCTAAAATCATCTTCTGGTATGTTTTG ACACGTGGAGTCCTTCGTCCCAGGGCCCCCTCGCCGTGCTCAGCCTTCTGAGAAGCAGTGTG CAGTGTGTGACCAACCACGCTGGTGCTCACCTGGCTGGAGCCGAACACTCTTTACTGCGT TATACTCCAATCTGAAGTATAACGTGTCTGTGTTGAATACTAAATCAAACAGAACGTGGTCC CCTGACAGCTCCAGAGAAGTGGAAGAGAAATCCAGAAGACCTTCCTGTTTCCATGCAACAAA TCATCACAAATTGGCCCACCAGAGGTGGCACTGACTACAGATGAGAAGTCCATTTCTGTTGT GTCTCTGGTGGTTTGCCTAAACCTGCAAACATCACCTTCTTATCCATCAACATGAAGA<mark>ATg</mark>T TGCCGCTGCCGCCGCTGCTGCTGCTGCTGGCGGCGCCTTGGGGACGGGCAGTTCCCTGT

FIGURE 62

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA62815

<subunit 1 of _, 442 aa, 1 stop</pre>

<MW: 49932, pI: 4.55, NX(S/T): 5

LGYASHLMEIFCDSEENTEGTSLTQQESLSRTIPPDKTVIEYEYDVRTTDICAGPEEQELSL CARTLKDQSSEFKAKIIFWYVLPISITV?LFSVMGYSIYRYIHVGKEKHPANLILIYGNEFD QIYSNLKYNVSVLNTKSNRTWSQCVTNHTLVLTWLEPNTLYCVHVESFVPGPPRRAQPSEKQ QEEVSTQGTLLESQAALAVLGPQTLQYSYTPQLQDLDPLAQEHTDSEEGPEEEPSTTLVDWD KRFFVPAEKIVINFITLNISDDSKISHQDMSLLGKSSDVSSLNDPQPSGNLRPPQEEEEVKH MSYNGLHQRVFKELKLLTLCSISSQIGPPEVALTTDEKSISVVLTAPEKWKRNPEDLPVSMQ PQTGRLCIPSLSSFDQDSEGCEPSEGDGLGEEGLLSRLYEEPAPDRPPGENETYLMQFMEEM

Important features:

Signal peptide:

amino acids 1-28

amino acids 140-163

Transmembrane domain:

N-glycosylation sites.

amino acids 71-74, 80-83, 89-92, 204-207, 423-426

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WO 00/12708

FIGURE 63

CCAGCCCGGCCCCTGCCTGGGACCACCAGGGCCCCCAGGAGAAGCCGCC<u>TGA</u>GCCACAACCT CCGGACGTCTGCAACAGCTCCTGGAAAGGGCCACCTGACACTTACCATGCTCTGCACCCGCAG GGCTTCCTGCGAGCCCGCTGGGTGGTCTCGGCCGCCCACTGCTTCAGCCACAGAGAGCCT GATGCTGCCCGTGAAGCCCCCCCCCCAGGCTCCTGGGGGGCCCAGATCATCGGGGGCCCACGAGG AAGCCTGATGTTCAGGGTTGGGGTGGGACGGGCAGCGGTGGGGCACACCCCATTCCACATGCA TGCGGCATGCAAATGAGATGGCCGCTCCAGGCCTGGAATGTTCCGTGGCTGGGCCCCACGGG GTGTACACGCAGGTGTCCGCCTTTGTGGCCTGGATCTGGGACGTGGTTCGGCGGAGCAGTCC TCGTGTCTGACTTTGAGGAGCTGCCGCCTGGACTGATGGAGGCCAAGGTCCGAGTGCTGGAC ATCTGCCTGCTGCGGCTGAACGGCTCTGCTGTCCTGGGCCCTGCAGTGGGGCTGCTGAGGCT TGTTTGGCATCGATGCTCTCACCACGCACCCCGACTACCACCCCATGACCCACGCCAACGAC TGACCCCCCACTCCAGGCCCTACATGGCATCCGTGCGCTTCGGGGGCCAACATCACTGCGGA CGGACGCGTGGGCGACGCGTGGGCCGGACGCGTGGGTCTCTGCGGGGAGACGCCAGCCTGCG ACCGGGCTCACGGCCTCGTTTCCTTCTCGGGGCCTCTGGTGCGGCGACCCCAAGACCCCCGAC TGGGGACAGCCACAGACGGGCTTCTGCTCGGCCGACTCCGGAGGGCCCCTGGTGTGCAGGA TCTGCC<u>ATG</u>GGGCTCGGGTTGAGGGGCTGGGGACGTCCTCTGCTGACTGTGGCCACCGCCCT

EIGURE 64

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA62845

><subunit 1 of 1, 283 aa, 1 stop

><MW: 30350, pI: 9.66, NX(S/T): 2

MGLGLRGWGRPLLTVATALMLPVKPPAGSWGAQIIGGHEVTPHSRPYMASVRFGGQHHCGGF
LLRARWVVSAAHCFSHRDLRTGLVVLGAHVLSTAEPTQQVFGIDALTTHPDYHPMTHANDIC
LLRLNGSAVLGPAGLLRLPGRRARPPTAGTRCRVAGWGFVSDFEELPPGLMEAKVRVLDPD
VCNSSWKGHLTLTMLCTRSGDSHRRGFCSADSGGELVCRNRAHGLVSFSGLWCGDPKTPDVY
TQVSAFVAWIWDVVRRSSPQPGPLPGTTRPPGEAA

Signal peptide:

amino acids 1-30

FIGURE 65

WO 00/12708

CATCCATGGCTCCACCTTCTCCAGCACCACACTCGGGCCCATCTTCTGGCTGCTGGTCAAGA
GCCCCGAGCTGGCCCAGCCAGCACATACCTGGCCGGAGGAACTGGCGGATGTT
TCCGGAAAGTACTTCGATGGACTCAAACAGAAGGCCCCGGGCCCCCGAGGCTGAGGATGAGGA
GGTGGCCCGGAGGCTTTGGGCTGAAAGTGCCCGCCTGGTGGCTTAGAGGCTCCTCTGTGA TTGCCTGGGACTCCCACCTTCCTATCAATTCTCATGGTAGTCCAAACTGCAGACTCTCAAAC GAGTTCAGGCTCTGCACGGCATGGAGTGGGAACCCCACCAGCTGCTGCTACAGGACCTGGGA GGTGTTTGCTGAGGGCTTCCTGTGCCAGAGCCCAGCCAGAGAGCAGGTGCAGGTGTCATCCC CTGTCTCCCATGATGGTGTGGTACAGCGAGCTGTTGTCTGGCTATGGCATGGCTGTGCCGGG GACTGGCGGCCGCATGCCCGCAGTAGGTTCTAGGGGGCGGTGCTGGCCGCAGTGGACTGGC GGGAGCAGCCCCTCCCCAGA<u>TAA</u>CCTCTGGAGCAGATTTGAAAGCCAGGATGGCGCCTCCAG GCCAGAGCANGCTCGCCATCGTCCTCTTCACCAAGGAGCTGAGCCGGCGGCGGCTGCAAGGCTCT **GCACATAGACTTTGACGACTTGAACTGGCAGACGAGGAAGTATAACACCAAAGCCGCCTACT** AAGCTGAAAGCCTCAGCCCCTTCGCGGATCATCAACCTCTCGTCCCTGGCCCATGTTGCTGG GGACATTCTAATCAACAACGCGGGTGTGATGCGGTGCCCCCACTGGACCACCGAGGACGGCT CGGCAGCAAAGGACATCCGCGGGAGACCCTCAATCACCATGTCAACGCCCGGCACCTGGAC GGAACTGGCCAGGAGAGGGAACATCATCCTGGCCTGCCGAGACATGGAGAAGTGTGAGG ATCCCTGGGAAGACGGTCATCGTGACGGGCGCCAACACAGGCATCGGGAAGCAGACCGCCTT CAGGCGCCGCCGTGCTGCTCAAGGACTATGTCACCGGTGGGGCTTGCCCCAGCAAGGCCACC TGTGCATGCATGGTCCTCTGAGCCTTGGTTTCTTCAGCAGTGAGATGCTCAGAATAACTG TCCGTGAAGAGCATGGGCAAGTTGTCTGACACTTGGTGGATTCTTGGGTCCCTGTGGGACCT TGTGCACTTGCAGGCCACGTCAGGAGAGCCAGCGGTGCCTGTCGGGGAGGGTTCCAAGGTGC AGGGGCCATCTGATGCTTCCCCTGGGAATCTAAACTGGGAATGGCCGAGGAGGAAGGGGCTC CTGCAGGTGAGCACTGCCCCGGGCTCTGGCTGGTTCCGTCTGCTCTGCTGCCAGCAGGGGAG ACCGAGGACAGCTGTCCGCCATGCCCGCAGCTTCCTGGCACTACCTGAGCCGGGAGACCCAG TCGAGATGCAGTTTGGCGTTAACCACCTGGGTCACTTTCTCTTGACAAACTTGCTGCTGGAC TTGGCTTCCCTCAAGTCTATCCGAGAGTTTGCAGCAAAGATCATTGAAGAGGAGGAGCGAGT CGCCTGTCCCCGGCCCGGC<u>ATG</u>AGCCGCTACCTGCCGCCGCTGTCGGCGCTGGGGCACGGTAC

FIGURE 66

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64842</pre>

><subunit 1 of 1, 331 aa, 1 stop

><MW: 35932, pI: 8.45, NX(S/T): 1

MSRYLLPLSALGTVAGAAVLIKDYVTGGACPSKATIPGKTVIVTGANTGIGKQTALELARRG
GNIILACRDMEKCEAAAKDIRGETLNEHVNARHLDLASLKSIREFAAKIIEEEERVDILINN
AGVMRCPHWTTEDGFEMQFGVNHLGHFLLTNLLLDKLKASAPSRIINLSSLAHVAGHIDFDD
LNMQTRKYNTKAAYCQSKLAIVLFTKEUSRRLQGSGVTVNALHFGVARTELGRHTGIHGSTF
SSTTLGPIFWLLVKSPELAAQPSTYLAVAEELADVSGKYFDGLKQKAPAPEAEDEEVARRLW
AESARLVGLEAPSVREQPLPR

Signal peptide: amino acids 1-17

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FIGURE 67

GGATGAGGCAAGTCTAGAAGATGCCTTGGATCACTTGGCCTTTGCTTATTTCCGGGCAGGAAATGTTTCTCTGCTGTGCCCTCAGCCTCTCCGGGAGTTTCTTCTCTACAGCCCAGATAATAAGAGG GAAGTTCGCGAGCGCTGGCAIgTGGTCCTGGGGCGCCTGGCGGCGCTGCTGGCGGCGTGCTG GCGCTCGGGACAGGAGACCCAGAAAGGGCTGCGGCTCGGGGCGACACGTTCTCGGCGCTGAC GCTGGCTGTCCTGTCCTGGTGGGAGATAAGTGGGTGGCCAACAAGTGGATACATGAGTATGG GGTGGAAGCTGGAGGAGCCACAGCCTTCATCTATGCCAACCTCAGCGTGCCTGTGGTTAGGAACTGCATCAT CCACCGCATTGCTGCCCTCACAGGCCTTGATGTCCGGCCTCCCTATGCAGAGTATCTGCAGG TACCGCATCAGCAAAAGTGCCTGGCTGAAGGACACTGTTGACCCAAAACTGGTGACCCTCAA GCCCTACATTGCTCTACCATGACTTCGTCAGTGACTCAGAGGCTCAGAAAATTAGAGAAC GAGACCAATTCCAACGCCTACCTGCTGCTCCAGCCCATCCGGAAGGAGGTCATCCACCTGGA ATTCCATGGCTGGAGGAGGCTGTCAGTCTCTTCCGAGGATCTTACGGAGAGTGGAAGACAGA CAGGGGATGACTGCTTCCAAGTTGGCAAGGTGGCCTATGACATGGGGGGATTATTACCATGCC TCAGAGAGTCACTGGCTCTGCCATCACTGACCTGTACAGCCCCAAACGGCTCTTTTCTCTCA GCCCTGATGCGGCTGCAGGACGTGTACATGCTCAATGTGAAAGGCCCTGGCCCGAGGTGTCTT ATGGCTATGAGAAGGTGGAGCAAGACCTTCCAGCCTTTGAGGACCTTGAGGGAGCAGCAAGG GTCTGACTGGAGGAATGTGGTACATAGTCTGGAGGCCAGTGAGAACATCCGAGCTCTGAAGG GAGGATTCAACAACCCCTGTGGCTAACCCTCTGCTTGCATTTACTCTCATCAAACGCCTGC CAGCGTGGCGCGCCCTGGCGCCCGAGCGCCGGCTGCTGGGGGCTGCTGAGGCGGTACCTG CAGGGAGTGTCCCCCTCCCAGAAGCATATCCCCAGATGAGTGGTACATTATATAAAGGATTTTT GGGCTAGCCTGACTCCCAGAACTTTAAGACTTTCTCCCCCACTGCCTTCTGCTGCAGCCCAAG AGTTCAGATACTCTGTTGGGAACAGGACATCTCAACAGTCTCAGGTTCGATCAGTTGGGTC GTCAGAGTAGGATGCACAGTACAAAGGAGGGGGGAGTGGAGGCCTGAGAGGGGAAGTTTCTGG **AAGGGAGAGGTTGTTACCAGGGGACACTGAGAATGTACATTTGATCTGCCCCAGCCACGGAA** tggtggagtcctgtggctttccagagaagccaggagccaaaagctggggtaggagaggagaa TGGTGAACTATGGCATCGGAGGACACTATGAGCCTCACTTTGACCATGCTACGTCACCAAGC TTGCAGAACCATGGCTACAGAGGTCAGTGGTGGCATCAGGGGAGAAGCAGTTACAAGTGGAG atgittataaatcaaaa TTTAAGTTGAAAACAACTTTCTTTTCTTTTGTATGATGGTTTTTTAACACAGTCATTAAAA TTTTGGCACTTTGAACCTTGACCACAGGGACCAAGAAGTGGCAATGAGGACACCTGCAGGAG

FIGURE 68

MGPGARLAALLAVLALGTGDPERAAARGDTFSALTSVAEALAPERRILGLLRRYLRGEEARL
RDLTRFYDKVLSLHEDSTTPVANPLLAFTLIKRLQSDMRNVVHSLEASENIRALKDGYEKVE
ODLFAFEDLEGAARALMRLQDVYMLNVKGLARGVFQRVTGSAITDLYSFKELFSLTGDDCFQ
VGKVAYDMGDYYHAIFMLEEAVSLFRGSYGEMKTEDEASLEDALDHLAFAXFRAGNVSCALS
LSREFLLYSFDNKRMARNVLKYERLLAESPNHVVAEAVIQRPNIFHLQTRDTYEGLCQTLGS
OPTLYQIPSLYCSYETNSNAYLLLQFIRKEVIHLEPYIALYHDFVSDSEAQKIRELAEFWIQ
RSVVASGEKOLQVEYRISKSAMLKDTVDFKLVTLAHRIAALTGLDVRPPYAEYLQVVNYGIG
GHYEPHFDHATSPSSFLYRMKSGNRVATFMIYLSSVEAGGATAFIYANLSVFVVRNAALFWM
NLHRSGEGDSDTLHAGCFVLVGDKWVANKWIHEYGQEFRRFCSSSFED

Signal peptide: amino acids 1-19

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FIGURE 69

TAATCAAAGCTGGTATTTCCCCGCATGTCTTATTCTTGCCCCTTCCCCCAACCAGTTTGTTAA GITTTTTTTTACGTGATTTTTGTAACATTCATTTTTTTTGTACAGATAACAGGAGTTTCTGAC GCATCTGGGGAAGGGCAGGGGAAGAGCTGTCCATGCAGCCACGCCCATGGCCAGGTTGGC GGCAGTTTTGTAGCACCTGTAATTGGGGAGAGGGAGTGTGCCCCTCGGGGCAGGAGGGAAGG GAGCCTGAGGCTCTGCTCAGGGCCCATTTCATCTCTGGCAGTGCCTTGGCGGTGGTATTCAA CCCAGGGAGCAGAGCCTGGGCCTCCCCTAAGAGGCTTTCCCCGAGGCAGCTCTGGAATCTGT TGGGATAGCACCTCTCAGTCAACATCGTGGGGCTGGACAGGGCTGCGGCCCCTCTGCCCACA ATGCTGCTTGTGCTACCCCAAT<u>TAG</u>GGCCCAGCCTGCCATGGCAGCTCCAACAAGGACCGTC TCCTGGGGGTGCTGCTGACGCTGCTGCACATCACCCGGGTGGAGGACATCATCATGGAGCAC CTGGTTCATGGACAACTACACCATCATGGCGTGCATCCTCCTGGGCATCCTGCTTCCCCAGT AAGGAGCGTTTCAGTGTGCAGGATGTCATCTACGTGCGGGGCTGCACCAACGCCGTGATCAT CCTGCTGCATCAGGAACACGACAGAAGTTGTCAACACCATGTGTGGCTACAAAACTATCGAC GAGCAAGAATCAGTACCACGACTGCAGTGCCCCTGGACCCCTGGCCTGTGGGGTGCCCTACA AACATCATGGACTTTGTTCAGAAAAAGTTCAAGTGCTGTGGCGGGGAGGACTACCGAGATTG ACTTCCTGAACGACAACATTCGAAGAGGAATTGAGAACTACTATGATGATCTGGACTTCAAA CTGCCTCATCATGGAGCTCATTGGTGGCGTGGTGGCCTTGACCTTCCGGAACCAGACCATTG GTGCTGGCGTCCCTCCGTGACAACCTGTACCTTCTCCAAGCATTCATGTACATCCTTGGGAT TGGCTCCAGCCATCATCCTCATCCTCCTGGGCGTCGTCATGTTCATGGTCTCCTTCATTGGT GTCTGTGGGCATCTATGCAGAGGTTGAGCGGCAGAAATATAAAAACCCTTGAAAAGTGCCTTCC TGGCTCAAGTTTTCACTTATCATCTATTCCACCGTGTTCTGGCTGATTGGGGCCCTGGTCCT **GAAGCCACCAGACTCCACGGTGTGGGGCCCAATCAGGTGGAATCGGCCCCTGGCAGGTGGGGCC** GAGATAGGGAGTCTGGGTTTAAGTTCCTGCTCCATCTCAGGAGCCCCTGCTCCCACCCCTAG

FIGURE 70

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64863</pre> ><subunit 1 of 1, 294 ma, 1 stop

><MW: 33211, pI: 5.35, NX(S/T): 3

NDNIRRGIENYYDDLDFKNIMDFVQKKFKCCGGEDYRDWSKNQYHDCSAPGPLACGVPYTCC AIILILLGVVMFMVSFIGVLASLRDNLYLLQAFMYILGICLIMELIGGVVALTFRNQTIDFL MPRGDSEQVRYCARFSYLMLKFSLIIYSTVFWLIGALVLSVGIYAEVERQKYKTLESAFLAP VLLTLLY ITRVED I IMEHSVTDGLLGPGAKPSVEAAGTGCCLCYPN IRNTTEVVNTMCGYKTIDXERFSVQDVIYVRGCTNAVIIWFMDNYTIMACILLGILLPQFLG

Signal peptide:

amino acids 1-44

Transmembrane domaine:

amino acids 22-42, 57-85, 93-116, 230-257

70/270

WO 00/12768

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FIGURE 71

GGAAGGCTGGGTCCCAGCTGGGAGTATGGGTGTGAGCTCTATAGACCATCCCTCTCTGCAAI AGCCTCCTTGTGGAAACCCAGCTCTCCTGTCTCCCAG<u>TGA</u>AGACTTGGATGGCAGCCATCAG AAGGCCTTGGGATTCGAGGCAGCTGAGTCCTCACTGACCAAGGATGCCCCTTGTGCTTACTCC ACTCCATCCTGCTGCCGAACCAGAATGGCAAATTAAGATCTGGGGTCCCAGTGTCATTGGTG GAACTCTGGGATTGGCTGGTTCCAACCTGATGTTCTGAAAAAACATCATCACTGAGATCATCC ACCAAAGGTGACCAACTTATACTCAACTTGAATAACATCAGCTCTGATCGGATCCAGCTGAT GTGAAGCCCTCCGCCCTTTGTTCACCCTGGGCATCGAAGCCAGCTCGGAAGCTCAGTTTTAC TTTTATAGACCAAGGCCATGCCAAGGTGGCCCAACTGATCGTGCTGGAAGTGTTTCCCTCCA GCTGCAGATAAGCTGGGATCTACCCAGATCGTGAAGATCCTAACTCAGGACACTCCCGAGTT ACTCTGTGCTTCCTGAGAGTGCCCATCGGCTGAAGTCAAGCATCGGGCTGATCAATGAAAAG GGACGTGGTGAAAGCTGCAGTGGCTGCTGTGCTCTCCAGAAGAATTCATGGTCCTGTTGG AGCTCTACCTGGGGGCCAAGTTGTTGGACTCACAGGGAAAGGTGACCAAGTGGTTCAATAAC CCTCAGCATTGACCGTCTGGAGTTTGACCTTCTGTATCCTGCCATCAAGGGTGACACCATTC ATCGAGGCTTCCTTCAATGGCATGTATGCAGACCTCCTGCAGCTGGTGAAGGTGCCCCATTTC AGGTCATGAACCTCCTAGTGCCATCCCTGCCCAATCTAGTGAAAAACCAGCTGTGTCCCGTG CGCATGGACACCAGTGCAAGTGGCCCCACCCGCCTGGTCCTCAGTGACTGTGCCACCAGCCA ACACGCCCTTGGTCAAGACCATCGTTGGAGTTCCACATGACGACTGAGGCCCAAGCCACCATC GCCCTCGGCCAATGACCAGGAGCTGCTAGTCAAGATCCCCCTGGACATGGTGGCTGGATTCA GTCCTGAAGCACATCATCTGGCTGAAGGTCATCACAGCTAACATCCTCCAGCTGCAGGTGAA TCAGTGCCATGCGGGAAAAGCCAGCCGGAGGCATCCCTGTGCTGGGCAGCCTGGTGAACACC AAAGCTGACACAGGAGCTGAAAGGACCACAACGCCACCAGCATCCTGCAGCAGCTGCCGCTGC TTGATCCAAGCCACCCTCAGTCCCACTGCAGTTCTCATCCTCGGCCCAAAAGTCATCAAAGA CACCTGGGAAGAT@GCCGGCCCGTGGACCTTCACCCTTCTCTGTGGTTTTGCTGGCAGCCACC GAGGAGCGGGCCGAGGACTCCAGCGTGCCCAGGTCTGGCATCCTGCACTTGCTGCCCTCTGA CAATAAACACTTGCCTGTGAAAAA TCTGCAGCTTCCCTGACAATGCCCACCCTGGACAACATCCCGTTCAGCCTCATCGTGAGTCA

FIGURE 72

><subunit 1 of 1, 484 aa, 1 stop ></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64881

><MW: 52468, pI: 7.14, NX(S/T): 3

LPNQNGKLRSGVPVSLVKALGFEAAESSLTKDALVLTPASLWKPSSPVSQ RPLFTLGIEASSEAQFYTKGDQLILNLNNISSDRIQLMNSGIGWFQPDVLKNIITEIIHSIL PESAHRLKSS IGLINEKAADXLGSTQIVKILTQDTPEFF IDQGHAKVAQLIVLEVFPSSEAL CAKLLDSQGKVTKWFNNSAASLTMPTLDNIPFSLIVSQDVVKAAVAAVLSPEEFMVLLDSVL LLVPSLPNLVKNQLCPVIEASFNGMYADLLQLVKVPISLSIDRLEFDLLYPAIKGDTIQLYL VKTI VEFHMTTEAQATIRMDTSASGPTRLVLSDCATSHGSLRIQLLYKLSFLVNALAKQVMN REKPAGGIPVLGSI,VNTVLKHIIWLKVITANILQLQVKPSANDQELLVKIPLDMVAGFNTPL MAGPWTFTLLCGLLAATLIQATLS PTAVLILGPKVIKEKLTQELKDHNATSILQQLPLLSAM

Important features of the protein:

Signal peptide:

amino acids 1-21

amino acids 48-51, 264-267, 401-404 N-glycosylation sites.

amino acids 412-415

Glycosaminoglycan attachment site.

LBP / BPI / CETP family proteins.

amino acids 407-457

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FIGURE 73

CCATACAGCTTTCTGATGAGT<u>TAA</u>AAAGGTCCCAGAGATATATAGACACTGGAGTACTGGAA ATTGAAAAAGCAAATCGTGTGTTTTTTTAAAAAAGAATGCAACTTGTATATTTTTTTATATTTTCAATAAGAAGAATGCAACTTGTATATTTTTTTACCCTTAACTCTTTAAATAGTTAATCATTTAACCAAAGAAGAAGATGTTAACCTTCTCTTAACAAAGCAATCCTCTCTTAACCTTCTCTTT GAGAATCACTTGAACTCAGGAGATGGAGGTTTCAGTGAGCCGAGATCACGCCACTGCACTCC AAAAATTAGCTGGGTGTGGCAGGAGCCTGTAATCCCAGCTACACAGGAGGCTGAGGCAC GAGGTCAGGAGTTCGAGACCATCCTGGCCAACATGGTGAAACCCCGGTGTCTACTAAAAATAT TCTCTAAATACAGGATTATAATTTCTGCTTGAGTATGGTGTTAACTACCTTGTATTTAGAAA GAACACCATTCTTCAGAGCACACGTCTAGCCCTCAGCAAGACAGTTGTTTCTCCTCCTCCTT TGTTACAGATAACTACATTAGGAATTCATTCTTAGCTTCTTCATCTTTGTGTGGATGTGTAT CTACTACTTYGTTTTAGTTAGAACAAAGCTCAAAACTACTTTAGTTAACTTGGTCATCTGAT CCCAGTGAACTTTATGGAACATTTAATTTAGTACAATTAAGTATATTATAAAAATTGTAAAA ATAAGAATCCCCACACGGGACATGTGAATTATATCCATGGAAGCAGTCAAGCCCAGTTTGTA TTTTGTGCTTGCTATGACATCTGGTCAAATGTGGAACCATATAAGAGGACCACCATATGCCC CTTCGAAGAAGTAATATGGAATTTCTCTTTAATAAAACTGGATGGGCTTTTGCAGCTTTGTG CAAATTATGCTGGTCCCCTTATGTTGGGATTGCTTTTGGCTGTTATTGGTGGACTTGTGTAT TGAGCAGATTGCCCGGTGGATCGCCGACAGAACTGATGTCAATATTAGAGTGATTAGACCCC CCTGCAAAAGGGAAACCCCAAACGGGGTGATACATATGAGTTACAGGTGCGGGGTTTTTTCAGC ATGAAGGCTCTGATGTATTTCAGATGCTAAACATGAATTCAGCTCCAACTTTCATCAACTTT <u> AAACTCCTGGCGATACTCCAGTGCATTCACCAACAGGATATTTTTTTGCCATGGTGGATTTTG</u> CTCCAACTGCATAGACAGTGTGTCGTTTGCAAGCAAGCTGATGAAGAATTCCAGATCCTGGC <u> AGTTCCGTCGCCTTGTGAAAGCCCCACCGAGAAATTACTCCGTTATCGTCATGTTCACTGCT</u> GAGCGAACATGGCAGCGCGTTGGCGGTTTTGGTGTGTCTCTGTGACCATGGTGGTGGCGCTG TTTATATTGCCTTATCCAAAGATGGGGAAAGTAAGTCCTGACCAGGTGTTCCCACATATGCC

FIGURE 74

MAARWRFWCVSVTMVVALLIVCDVPSASAQRKKEMVLSEKVSQLMEWTNKRPVIRMNGDKFR
KLVKAPPRNYSVIVMFTALQLHRQCVVCKQADEEFQILANSWRYSSAFTNRIFFAMVDFDEG
SDVFQMLNMNSAPTFINFPAKGKPKRGDTYELQVRGFSAEQIARWIADRTDVNIRVIRPPNY
AGPLMLGLLLAVIGGLVYLRRSNMEFLFNKTGWAFAALCFVLAMTSGOMWNHIRGPPYAHKN
PHTGHVNYIHGSSQAQFVAETHIVLLFNGGVTLCMVLLCEAATSDMDIGKRKIMCVAGIGLV
VLFFSWMLSIFRSKYHGYPYSFLMS

Signal peptide:

amino acids 1-29

Transmembrane domains:

amino acids 183-205, 217-237, 217-287, 301-321

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FIGURE 75

CAAAAACCTGCATCCACCCTGGATTCTGAGTGAATTCCATGGATGTAATGTGAATGCCTCCA
CCTACATGCTTCGAACTAACCACTGGAATATTATAGCCTATTCGGATGGTGCATCAATATTTG
CCTCAACTCTTTGATCTTTCCTCGGATCCAGATGAATTAACAAATGTTGCTGTAAAATTTTCC
AGAAATTACTTATTCTTTGGATCAGAAGCTTCATTCCATTATAAACTACCCTAAAGTTTCTG TTACCCTTCACCATCTTCTGGAGAAAATTTTGGATCTTCAACATTTCACAGATCTCTTTATT
GGCTTGAAAAAGTGTCTCATGATGCCATCAAAATCCCCAAAGTGGTCACCTTTGTCAGAAATG
CACCCTGTAGATTATTACTCTTCTTATACAAAAAACTGCACTGGAAGATTTACAÁAAAAAGA TGAAAATGCAATTGATCAGTGGCTTAAAACCCCATATGAATCCAAGAGCAGTT<u>TGA</u>ACAAAAA GGGAAACTGGACTATACTTCAGGACATCACTCCATTAGTAATCGTGTGGAAGCGTGGACAAG CAACATGGTGAAACCCTGTCTCTACTAAAAATACAAAAATTAGCTGGGCGCGGTGGTGCACA CCAGGACTTTGGGAGGCTGAGGAAAGCAGATCACAAGGTCAAGAGATTGAGACCATCCTGGC GTTTAAAAATAGTGTTCTAGAGATACATATAAATATATTACAAGATCATAATTATGTATTTT TATTCAAACGTTATAGCAAATCTTAGGTGGCACCAAGACTGGCAGAAGGAACCAAGGAAGTA TGGTTTCTTGTGGATATTTACCCTACCATGCTTGATATTGCTGGAATTCCTCTGGCTCAGAACCTTGATGATGATGAATACATTTAAGAATGAACATTAAAGA AAATTATTTTGGCCCTTCATCAATTAGATCTTCTTCAGAAAACTATTGTCATATACTCCTCA CTAAAGTCAGAGTGATGGAAAGGGATTGGCAGAATACAGACAAAGCAGTAAACTGGTTAAGA ATCCAAATTATACAACATGGATGGATGTCATGGAGAGGCATGGCTACCGAACACAGAAATTT GAACGCCAGAGGGGAGGCGGCTGGCCCGGCGGCAGGCTCTCAGAACCGGCTACCGGCG<u>ATG</u>CTA GGCCTTTGTACAATTTCTAACAATTTAGTGGAAGTATCAAAAGGATTGAAGCAAATACTGTA TTGCAGTGAGCTGAGATTGCGCCACTGTACTCCAGCCTGGCAACAGAGTGAGACTGTGTCGC CCTATAGTCTCAGCTACTCAGAGGCTGAGGCAGGAGGATCGCTTGAACCCGGGAGGCAGCAG AAATGAAACAGTTTTAATAATTACCAAGTTTTGGCCGGGCACAGTGGCTCACACCTGTAATC CTTCTGTCCACCAGTATAATAAAGAGCAGTTTATCAAGTGGAAACAAAGTATAGGACAGAAT TGCACATGTTCCGCTTTTGATGATGGGACCAGGAATTAAAGCCGGCCTACAAGTATCAAATG GACCATGGAGAGCTGGCCATGGAACATCGACAGTTTTATAAAATGAGCATGTACGAGGCTAG aattaagaatattagagcattttattatgctatgtgtgctgagacagatgccatgcttggtg aaggaagcaattaattacactgaaccatttgttatttacttgggattaaatttaccacaccc AGATGTTGCTTTCTTACTCAGACAAGAAGGCAGGCCCATGGTTAATCTTATCCGTAACAGGA AGCAATGTGGAGTGGCCTCTTCACTCACTTAACAGAATCTTGGAATAATTTTAAGGGTCTAG ACACGTGGGACTTCCTTTCTGAATGCCTACACAAACTCTCCAATTTGTTGCCCCATCACGCGC gaaggttaacatttcatccaggaagtcaggtagtgaaacttccttttatcaactttatgaag GCAGAGGCGGAGAGCAGCCAAAGCGCCCAATGTGGTGCTGGTCGTGAGCGACTCCTTCGATG CTGCTGTGGGTGTCGGTGGTCGCAGCCTTGGCGCTGGCGGTACTGGCCCCCGGAGCAGGGGA AAGCAACCAAACTGCAAGCTTTGGGAGTTGTTCGCTGTCCCTGCCCTGCTCTGCTAGGGAGA acagttatgttcctttaaataatagagaatataaaatattgtaataatatatatatatatat TATTTTAAGATAAAATGCCAATGATTATAAAATCACATATTTTCAAAAATGGTTATTATTTA

FIGURE 76

</usr/seqdb2/sst/DNA/Dnasegs.min/ss.DNA64885
<subunit 1 of 1, 536 aa, 1 stop

<MW: 61450, pI: 9.17, NX(S/T): 7

MLLIWYSVVAALALAVLAPGAGEQRRRAAKAPNVVLVVSDSFDGRLIFPHPGSQVVKLPFINF
MKTRGTSFLNAYTNSPICCPSRAAMMSGLFTHLTESWNNFKGLDPNYTTWMDVMERHGYRTQ
KFGKLDYTSGHHSISNRVEAWTRDVAFLLRQEGRPMVNLIRNRTKVRYMERDWQNTDKAVKW
LRKBAINYTEPFVIYLGLNLPHPYPSPSGGENFGSSTFHTSLYWLEKVSHDAIKIPKWSPLS
EMHPVDYYSSYTKNCTGRFTKKBIKNIRAFYYAMCAETDAMLGEIILALHQLDLLQKTIVIY
SSDHGELAMEHRQFYKMSMYEASAHVPLLAMGFGIKAGLQVSNVVSLVDIYFTMLDIAGIPL
PQNLSGYSLLPLSSETFKNEHKVKNLHPPWILSEFHGCNVNASTYMLRTNHWKYĮAYSDGAS
ILPQLFDLSSDPDELTNVAVKFPEITYSLDQKLHSIINYPKVSASVHQYNKEQFIKWKQSIG
QNYSNVIANLRWHQDMQKEPRKYENAIDQMLKTHMNPRAV

Important features: Signal peptide:

amino acids 1-15

N-glycosylation sites. amino acids 108-111, 166-169, 193-196, 262-265, 375-378, 413-416, 498-501

Sulfatases proteins: amino acids 286-315, 359-369, 78-97

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FIGURE 77

CAGAGAAATCGCTCCAACTACTACGATGCCTACCAAGCCCAACCTCTTGCCACAAGGAGCTC GCATTATTTCTTCCCTGTTCTCCCTGATAGCTGGAATCATCCTCTGCTTTTTCCTGCTCATCC CTTCTACTCACCACTGGTGCCTGACAGCATGAAATTTGAGATTGGAGAGGCTCTTTACTTGG GATGCAGGATGGGAGGACAGGAAGGCAGCCTGGGACAITTAAAAAAATA AGACTAATTTGTGCATGAACTGAAATAAAACCATCCTACGGTATCCAGGGAACAGAAAGCAG TCCAAAGAAACTGATTGGCCCTGGAACCTCCATCCCACTCTTGTTATGACTCCACAGTGTCC GGATGGGAAGGAGGAGTGGCTTTTGTGGGCATTGCTCTAACCTACTTCTCAAGCTTCCC ACTGACCCTCTGTGATCAAAGACCCTCTCTCTGGCTGAGGTTGGCTCTTAGCTCATTGCTGG ATCCCTTTGCCCTCTGGTTTACCTGGGACTCCATCCCCAAACCCACTAATCACATCCCACTG CCCTGCCCTAAGTCCCCAACCCTCAACTTGAAACCCCATTCCCTTAAGCCAGGACTCAGAGG CAGGTTGAATTGCCAAGGATGCTCGCCATGCCAGCCTTTCTGTTTTCCTCACCTTGCTGCTC ATAGACTGACTTTGGCCATTGGATTGAGCAAAGGCAGAAATGGGGGGCTAGTGTAACAGCATG CACCCCGAGGGCCACAGGTGAGGGACACTACCACTGGATCGTGTCAGAAGGTGCTGCTGAGG TCCAAGGCCTGGTCAACCTCCCAAAGTCAAGAGTGAGTTCAATTCCTACAGCCTGACAGGGT ATCCTTGGAGGCCTCCTGGGATTCATTCCTGTTGCCTGGAATCTTCATGGGATCCTACGGGA CAGTCTTCTGCCAGGAATCCCGAGCCAAAGACAGAGTGGCGGTAGCAGGTGGAGTCTTTTTC GGTGACATCCAGTGCAATCTCCTCCCTGGCCTGCATTATCTCTGTGGTGGGCATGAGATGCA TGTGACATCTATAGCACCCTTCTGGGCCTGCCCGCTGACATCCAGGCTGCCCAGGCCATGAT GGTTGCCATGCTGCTCCCCAGCTGGAAAACAAGTTCTTATGTCGGTGCCAGCATTGTGACAG GCCTCTCTTGGCCTCCAACTTGTGGGCTACATCCTAGGCCTTCTGGGGCTTTTTGGGCACACT AGCTTCAGCCTGAAGACAAGGGAGCAGTCCCTGAAGACGCTTCTACTGAGAGGTCTGCC<u>ATG</u> GAGAGAAGTCAGCCTGGCAGAGAGACTCTGAAATGAGGGATTAGAGGTGTTCAAGGAGCAAG

FIGURE 78

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64886
><subunit 1 of 1, 230 aa, 1 stop
><MM: 24549, pI: 8.56, NX(S/T): 1

MASLGLQLVGYILGLLGLLGTLVAMLLPSWKTSSYVGASIVTAVGFSKGLMWECATHSTGIT
OCDIYSTLLGLPADIQAAQAMWYTSSAISSLACIISVVGNRCTVFCQESRAKDRVAVAGGVF
FILGGLLGFIPVAWNLHGILKDFYSPLVPDSMKFEIGEALYLGIISSLFSLIAGIILCFSCS</pre>

Important features of the protein: Signal peptide:

SQRNRSNYYDAYQAQPLATRSSPRPGQPPKVKSEFNSYSLTGYV

amino acids 1-24

Transmembrane domains:

amino acids 82-102, 117-140, 163-182

N-glycosylation site.

amino acids 190-193

PMP-22 / EMP / MP20 family proteins.

amino acids 46-59

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FIGURE 79

FIGURE 80

MVPRIFAPAYVSVCLLLLLCPREVIAPAGSEPWLCQPAPRCGDKIYNPLEQCCYNDAIVSLSE TRQCGPPCTFWPCFELCCLDSFGLTNDFVVKLKVQGVNSQCHSSPISSKCESRRRFP

Signal peptide: amino acids 1-25

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FIGURE 81

FIGURE 82

MAPRIGCI VAVFAL I FOLISKLL CSHGAPVA PMTPYLML CQPHKR CGDKFYD PLQHCCYDD AVVP LARTOT CGNCTFRVCFBOCCPWTFMVKI. I NQNCD SARTSDD RLCRSVS

Signal peptide: amino acids 1-24

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FIGURE 83

GGCAGGTGCATTTGAGCCAGGGCTGGCTCTGTGAGTGGCCTCCTTGGCCTCGGCCTGGTTCCTCCTCTGTGACCCTCTGGGCTCAACCCCTCCTCCTGCTCTCTGGGCTCAGATACTGTGACATCCCAGAAGCCCAGCCCCTCAACCCCTCTGAATGCTAATGCTAATGCAATGCTAAGATTTTTGGGGTGCTGAGATTCTCCCCAAGTGACTTACATCATTAAGAA CCGGCTTTGAAGCCTCACCACCTGCCCAGGGGATACCCGAGGCCAAAGTCAGGCACCCCTG
TCCTATGTGGCCCAGCGGCAGCCTTCTGAGTCTTGGGCGGCATCTTGCTTTCGGAGCCCAGCAC
CCCCCTGTCTCCCCAGGCCCCCGGAGACGTCTTCTTCCCATCCCTGACCCTGACC GCATCAGTGGGACAAGATGGACACTGGGCCACCCTCCCAGGCACCAGACACAGGGCACGGTG CTCCAAACTTTGAGGTCATC<u>TAG</u>CCCAGCTGGGGGACAGTGGGCTGTTGTGGCTGGGTCTGG CTCCAACCGCCGTGCCCAGGAGCTGGTGCGGATGGACAGCAACATTCAAGGGATTGAAAACC ACCCATCCTCCCCAGGATAGTGAAAACATCACGGCTGCAGCCCTGGCTACGGGTGCCTGC CCATGGTGCCATGGAGCTGCAGGTGCAGACAGGCAAAGATGCACCATCCAACTGTGTGGTGT GATAGCGGCCTCTACTGCTGCCTGGTGGTGGAGATCAGGCACCACCACTCGGAGCACAGGGT CCTGCACCATGGAGGCCACCAGGCTGCCAACACCAGCCACGACCTGGCTCAGCGCCACGGGC GGCGAGGTGCAGACCTGCTCAGAGCGCCGGCCCATCCGCAACCTCACGTTCCAGGACCTTCA GCGCGTCCGACGGCGAC<u>ATG</u>GGCGTCCCCACGGCCCTGGAGGCCGGCAGCTGGCGCTGGGGA ATATTGGGGCATGGTGGCCTCCGTGAGCAAATGGTGTCTTGGGCAATCTGAGGCCAGGACAG CTGGGGCTTCCACTGCCTGCATTCCAGTCCCCAGAGCTTGGTGGTCCCGAAACGGGAAGTAC ACCTTCCCCAGCTGCCTCCTACCAGCAGTTTCTCTGAAGATCTGTCAACAGGTTAAGTCAAT GAGAGACTICICCCCCGIGGCCGCCTTGGCTCCCCCGTTTTGCCCGAGGCTGCTCTTCTGTC GTCTCAGAACGTCCAGCCCTTCAGCAGCTCTCGTTCTGAGACATGAGCCTTGGGATGTGGCA TGGAGTCGGCCTCCGACCACCATGGCAACTTCTCCATCACCATGCGCAACCTGACCCTGCTG TGGGCCCTGTGGACAAAGGGCACGATGTGACCTTCTACAAGACGTGGTACCGCAGCTCGAGG CACGCCGTATTCCCTGTATGTCTGTCCCGAGGGGCAGAACGTCACCCTCACCTGCAGGCTCT TOGOGGAGGCTTCCCCGCGCGCGGCGCGTCCCGGCTCCCCGGCACCAGAAGTTCCTCT ICCCIGCICTICGCICTCTICCIGGCIGCGICCCIAGGICCGGIGGCAGCCIICAAGGICGC

FIGURE 84

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64897

><subunit 1 of 1, 311 aa, 1 stop

><MW: 33908, pI: 6.87, NX(S/T): 6

MGVPTALEAGSWRWGSLLFALFLAASLGPVAAFKVATPYSLYVCPEGQNVTLTCRLLGPVDK GHDVTFYKTWYRSSRGEVQTCSERRPIRNLTFQDLHLHHGGHQAANTSHDLAQRHGLESASD HHGNFSITMRNLTLLDSGLYCCLVV2IRHHHSEHRVHGAMELQVQTQKDAPSNCVYPSSSQ DSENITAAALATGACIVGILCLPLILLLVYXQRQAASNRRAQELVRMDSNIQGIENPGFEAS PPAQGIPEAKVRHPLSYVAQRQPSESGRHLLSEPSTPLSPPGPGDVFFPSLDPVPDSPNFEVI

Signal peptide:

amino acids 1-28

Transmembrane domain: amino acids 190-216

FIGURE 85

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CAAAGTGACCAAGACATAACAAAGACC<u>TAA</u>CAGTTGCAGATATGAGCTGTATAATTGTTGTT GAAGGTCACTGGAACGTCTTCCTAGCCCAGACCCTGGAGCTGAAGGTCACGGCCAGTCCAGA AAGTCAGGAAGCAAGACTTCCAGAAAGAGGCACAGCACTTCCGACTGCTCGCTGGCCCCCAC AGAGGTGAAGTACCTGGCCCAAGGCCACACAGCCAGAATCTTCCACTTGACTCAGATCAAGA CGTCCACACATCGGTATCCCCAAGCCCAGACAACCTGCGTCGCTTTGCCCTGGAACACGAGG GCAGACCCTGGCCACAGTGAGATCAGTTCTACCAGGTGTCCCAAGGCACCGGGCCGGGTCCT CATCCTATGCACCTGTGAGGATGGCCGCCAGGACTGCCAGCGTGTGACCTGTCCCACCGAGT GCAGCACAACTGTCAAGATCGTCCTGAAGGAGAAACATAAGAAAGCCTGTGTGCATGGCGGG AGACATCCTCAGGATCCATGTTCCAGTGATGCTGGGAGAAAGAGAGGGCCCGGGCACCCCAGC GCAAAGATGAGGCAAGTGAGCAATCGGATGAAGAGGACAGTGTGCAGTCGCTCCATGGGGGTG AACCTGCCCGAACCAGGCTGCCCAGCACCCCTCCCACTGCCAGACTCCTGCTGCCAAGCCT CCTCGGACTTGGTGCAGATCTACCTCTGGAAGCTGGTAAAAAGATGAGGAAACTGAGGCTCAG ACCCCTGCCGTCACCCCGAGAAAGTGGCTGGGAAGTGCTGCAAGATTTGCCCAGAGGACAAA AAGACGTACTCCCACGGGGAGGTGTGGCACCCGGCCTTCCGTGCCTTCGGCCCCTTGCCCTG CCCCACTGGCCTCAGCGCCCCTCTGAGCTTCATCCCTCGCCACTTCAGACCCAAGGGAGCAG CGCCTGCCCAACCAGTGTGTCCTCTGCAGCTGCACAGAGGGCCAGATCTACTGCGGCCTCAC AGCACAACGGGACCATGTACCAACACGGAGAGATCTTCAGTGCCCATGAGCTGTTCCCCTCC CTGTCCCAAGTGTGTGGAACCTCACACTCCCTCTGGACTCCGGGCCCCACCAAAGTCCTGCC TGTTACCGCCTCCACTGTCCGCCTGTCCACTGCCCCCAGCCTGTGACGGAGCCACAGCAATG TGGAGCCACAAGGCCTGATGTACTGCCTGCGCTGTACCTGCTCAGAGGGCGCCCATGTGAGT AGACATGTTCTGCCTTTTCCATGGGAAGAGATACTCCCCGGCGAGAGCTGGCACCCCTACT CTCCGCTCCCGGACCAGCGGCCTGACCCTGGGGAAAGG<u>ATG</u>GTTCCCGAGGTGAGGGTCCTC TTTCCTGCCCACCGCTGCTTCCTGGCCCTTCTCCGACCCCGCTCTAGCAGCAGACCTCCTGG TICCCCGCGITCTCTTTCCACCTTTCTCTTCTTCCCACCTTAGACCTCCCTTCCTGCCCTCC

FIGURE 86

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64902</pre>

><gubunit 1 of 1, 451 aa, 1 stop

><MW: 49675, pI: 7.15, NX(S/T); 1

WYPEVRVLSSLLGLALLMFPLDSHARARPDMFCLFHGKRYSPGESWHPYLEFQGLMYCLRCT
CSEGAHVSCYRLHCPPVHCPQPVTEPQQCCFRCVEPHTPSGLRAFPKSCOHNGTMYQHGEIF
SAHELFPSRLPNQCVLCSCTEGQIYCGLTTCPEPGCFAPLFLPDSCQACKDEASEQSDEED
SVQSLHGVRHPQDPCSSDAGRKRGFGTPAPTGLSAFLSFIPRHFRPKGAGSTTVKIVLKEKH
KKACVHGGKTYSHGEVWHPAFRAFGPLPCILCTCEDGRQDCQRVTCPTEYPCRHPEKVAGKC
CKICPEDKADPGHSEISSTRCFKAPGRVLVHTSVSPSPDNLRRFALEHEASDLVEIYLWKLV
KDEETEAQRGEVPGPRPHSONLPLDSDQESQEARLPERGTALPTARWPPRRSLERLPSPDPG
AEGHGQSRQSDQDITKT

Signal peptide: amino acids 1-25

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FIGURE 87

GURE 88

MDSLRKMLISVAMLGAGAGVGYALLVIVTFGERRKQEMLKEMPLQDPRSREEAARTQQLLLA TLOEAATTQENVAWRKNWMVGGEGGASGRSP

Signal peptide: amino acids 1-18

PCT/US99/20111

TCAGTGTCCTGAGGAACAGGACTTTCTCCACATTGTTTTGTATTGCAACATTTTGCATTAAA GCTCTAACCTTGTATGCGGGCAGGCCAGGGAGCAGGCAGTGTTCTTCCCCCTCAGAGTG TCATACGGAACTCCAGATCCTGAGTAATCCTTTTAGAGCCCGAAGAGTCAAAACCCTCAATG TTGTGGCTCAAATCCTCTATATTTTTTAGCCAATGGCAATCAAATTCTTTCAGCTCCTTTGTT GATGAGGAAGAAGAGGAGGAGGTT<u>TGA</u>GGAGCTAGCCTTGTTTTTTTGCATCTTTCTCACTC AACCCCCGAGAACGCCAGCTCTATGCCTGGGATGATGGCTACCAGATTGTCTATAAGCTGGA CACCCGTCCTGCCAGTCGGGCCCCGCATCCAGTGCTCCTTTGATGCCAGCGGCACCCTGACCC ACTTGTGTCTGGCCAAGTTAGATCCACAGACACTGGACACAGAGCAGCAGCAGTGGGACACACCA GTGAGATGGAGAACACTTTGCAGCTAATCAAATTCCACCTGGCAAACCGGAACAGTGGTGGAC TTCCCTCCTGCTCCTGCCCCATGTCAACAAATTTCAGGCTAAGGATGCCCCAGACCCAGG CCATACATTTATATTATATCCCCACTAAATTTCTTGTTCCTCATTCTTCAAATGTGGGCCAG CTGAACGGGCAGCACTCCCTTATTTTCCCCGGAGATATGGTGCCCATGCCAGCCTCCGCTAT TGTCCCAGAGAGAATGCTGAGGCTGCCTTTGTCATCTGTGGGACCCTCTATGTCGTCTATAA CGACCTGGTAGCTGATGAGGAAGGTCTTTGGGCTGTCTATGCCACCCGGGAGGATGACAGGC AGCTCAGTATTCCCAGCAGAGGGGCTGATCCCCCCCTACGGCTTGACAGCAGACACCTACAT GCTGGTATATGGTGGCTTTCTTTATTTTGCTCGGAGGCCTCCTGGAAGACCTGGTGGAGGTG GCCATGGCTGCCCGGAAAGCTTCCCGAGTCCGGGTGCCCTTCCCCCTGGGTAGGCACAGGGCA TGTTAGATGGGACACAGAATGACACAGCCTTTGTCTTCCCAAGGCTGCGTGACTTCACCCTT ATTTGGTGGCCCAGCTGGTCTATGGACCAAGGATCCACTGGGGCAAACAGAGAAGATCTACG GATATGGTGACAGACTGTGGCTACACAATCTCTCAAGTGAGATCAATGAAGATTCTGAAGCG GTGGCAGAGAGGGAGGCAGGCACTCAGAACTGAGGCCGACACCATCTCCGGGAGAGTGGA аллаллалаааааааааа TTGATGAGAAGGTGACTGGAGGCCCTGGGACCAAAGGCAAGGGAAGAAGGAATGAGAAGTAC TCGTCTGGAGCGGGAGGTAGACTATCTGGAGACCCAGAACCCAGCTCTGCCCCTGTGTAGAGT AGAGTAGTCGGCATGCTGAGCTGCGGGACTTCAAGAACAAGATGCTGCCACTGCTGGAG TGTGGAGTACATGGAACGCCGACTAGCTGCTTTAGAGGAACGGCTGGCCCAGTGCCAGGACC CCTCTCCTCATCTTGTTCCTTTTGTCATGGTCGGGACCCCTCCAAGGACAGCAGCACCACCT ${\tt GGCTGACTGTACGTTCTACTCTGGCACCACTCTCCAGGCTGCC} {\tt ATGGGGCCCAGCACC}$ CAGGAGAGAAGGCACCGCCCCACCCCCGCCTCCAAAGCTAACCCTCGGGCTTGAGGGGAAGA

FIGURE 90

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64305
<subunit 1 of 1, 406 aa, 1 stop

<MW: 46038, pI: 6.50, NX(S/T): 2

MGPSTPLLILFLLSWSGPIQGQQHHLVEYMERRLAALEERLAQCQDQSSRHAAELRDEXNKM
LPLLEVAEKEREALRTEADTISGRVDRLEREVDYLETQNPALPCVEFDEKVTGGPGTKOKGR
RNEKYDMVTDCGYTISQVRSMKILKRFGGPAGLMTKDPLGQTEKIYVLDGTQNDTAFVFPRL
RDFTLAMAARKASRVRVPFPWVGTGQLVYGGFLYFARRPPGRPGGGGEMENTLQLIKFHLAN
RTVVDSSVFPAEGLIPPYGLTADTYIDLVADEEGLMAVYATREDDRHLCLAKLDPQTLDTEQ
QWDTPCPRENAEAAFVICGTLYVVYNTRPASRARIQCSFDASGTLTPERAALPYFPRRYGAH
ASLRYNPRERGLYAWDDGYQIVYKLEMRKKEEEV</pre>

Important features:
Signal peptide:
amino acids 1-21

N-glycosylation sites.
amino acids 177-180, 248-251

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FIGURE 91

CGGCATGCTCATCTGAGCCGAGAGGTGGAATCCAGGGTACAGATAGGAGATACCTTTTTTGGA GCCTATATCGTGGCACCTGGCTACCAAAGTACTGGGAATACTCTGCTGTTGGCCTATTTTTTG GCATTGTTGGACTGAAGATTTTCTTCTCCAAATTCCAGTGGAAAATCCAGGCGGAACTGGAC TTAGATCTTATTGATGACAGAGTGTATCCTAATGGTTTGTTCATTATATTACACTTTCAGTA AGTTTGCTCTCACTCCATCTGGCTAAGTGATCTTGAAATACCACCTCTCAGGTGAAGAACCG gatecaaagtecegeageageegecaaggtggetteeagatgaagggggaetggeetgtee AATCCCAGAGACAAGCAACAGTGAGTCCTCCTCACAGGCAACCACGCCCTTCCTCCCCAGGG ATAGTCATCTGCCCAGTCACCCAGGAATCAGAGAAAGAGGCCTCTTGGCAAAGGGCCTCTGC TCTGGATCCAGAGACGGCTCACCCGAAGCTCTGCGTTTCTGATCTGAAAACTGTAACCCATA
GAAAAGCTCCCCAGGAGGTGCCTCACTCTGAGAAGAGATTTACAAGGAAGAGTGTGGTGGCT TGGAGAAGAAAGCACGGACAGGCAGAATTGAGAGACGCCCGGAAACACGCAGTGGAGGTGAC TGTTTGATGTGGAGATCTCTGTGACCGTCCAAGAGAACGCCGGGAGCATATCCTGTTCCATG TCCTAAGACCAATGCAGAGGCCATGGAAGTGCGGTTCTTCAGGGGCCAGTTCTCTAGCGTGG GGGCCAGACAAGCCTGTCCAGGCCTTGGTGGGGGAGGACGCAGCATTCTCCTGTTTCCTGTC CTCTCATGCTCAGTTTGGTTCTGAGTCTCCTCAAGCTGGGATCAGGGCAGTGGCAGGTGTTT GACAGCTGTGTCTCGATGGAGTAGACTCTCAGAACAGCGCAGTTTGCCCTCCGCTCACGCAC TCAGGAATTCCCATCTCACAGGCTGTGGTGTAGATTAAGTAGACAAGGAATGTGAATAATGC CCGTCACCTCTCCTGTCATCCGTTTCCATGCCGTGAGGTCCATTCACAGAACACATCC<u>ATG</u>G AGCCTCTCCGTGGCTTCCGCACCTTGAGCATTAGGCCAGTTCTCCTCTTCTCTCTAATCCA1 ITGAAGGCTTATTGAGGCCCTACATTGAGTATCCGTCCTATAATGAGCAAAATGGAACTCCC

EIGURE 92

MALMLSILVI.SILKIGSGOMQVFGPDKFVQALVGEDAAFSCFLSPKTNAEAMEVRFFFRGQFSS
VVHLYRDCKDQPFMQMPQYQGRTKLVKDSIAEGRISLRIENITVLDAGLYGCRISSQSYYQK
AIMELQVSALGSVFLISITGYVDRDIQLLCQSSGMFPRPTAKWKGPQGQDLSTDSRTNRDMH
GLFDVEISITVQENAGSISCGMRHAHLSREVESRVQIGDTFFEPISMHLATKVLGILCCGLF
FGIVGLKIFFSKFQMKIQAELDMRRKHGQAELRDARKHAVEVTLDPETAHPKLCVSDLKTVT
HRKAPQEVPHSEKRFTRKSVVASQSFQAGKHYMEVDGGHNKRWRVGVCRDDVDRRXEYVTLS
PDHGYWVLRLNGEHLYFTLNPRFISVFPRTPPTKIGVFLJYECGTISFFNINDQSLIYTLTC
RFBGLLRPYIEYPSYNEQNGTPIVICPVTQESEKEASWQRASAIPETSNSESSSQATTPFLP
RGEM

Signal peptide:

amino acids 1-17

Transmembrane domain: amino acids 239-255

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FIGURE 93

CACTTGAGGCCAGGAGTTCTAGATGAGCCTGGCCAGCACAGTGAAACCCCGTCTCTACTAAA AGGCTGGGCGCGCTGGCTCACGCCTGTAATCCTAGCACTTTGGGAGGCCAAGGCGGGTGGAT TAAATGATATTATACTGTTATGGAATATTGTATCATATTGTAGTTTATTAAAAATGTAGAAG TTCTGGTTTGTTTTAATTTCAAAGGAATATTATGGACTGAAATGAGAGAACATGTTTTAAGA GTTGTTGTGAAGATTAAATGAGTTGATATATATAAAATGCCTAGCACATGTCACTCAATAAA CACTTACGAGCTGTGTTCCTTGGGCAAGTAATTTCCTTTCACTGAGCTTGTTTCTTCTCAAG TATATTTAATGTCAGGATTTAAAAACATCTAATTTACTGATTTAGTTCTTCAAAAGCACTAG GAGGATGAGGGTCATAGATTTACAAAATATTTTATATACTTTTATTCTCTTACTTTATATGT ACATGGAGCTCTCAGCATACCGTGCAACAGG<u>TAA</u>GCAACAGAGGGTGGAACTGAÁGTTTATT TTATTTTAGCAAGGGAAAAAAAAGGCTGCTACTCTAAGGACCATACTGGTTTAAACAAAG TGCAAAGAGGGCTTTTACCTAAATTACACTTCTGGGCTCTGTCAGCCATGTGACTGTAGTCC GCAACCAGACCACAGGGCAGTGTGAGTGTCGGCCAGGTTATCAGGGGCTTCACTGTGAAACC CGCCGACCACCCCTGTAGCGACCACCGTACCGGCGCCCACGACTCCCCGGACCCCGACCCCC ACCACCTTTCAGGCGCCGCTCGGCCCTCGCCGACCACCCCTCCGGCGGCGGCGAAACGCACTTC CGACTTCTCCAGCCCAGTCCCCGGAGACCACCCCTCTTTGGGCGACTGCTGGACCCTCTTCC GACCCGTCGCCGGGCCCGGGGTTGCGGGGGCGAGCCCAGCCACCCCTTCCCTAGGGCGACGGC GCGATGGTGCGCCCGGTGGCGGTGGCGGCGGTTGCGGAGGCTTCCTTGGTCGGATTGC actitagciccitgacaaagaagtgcittatactitagcactaaatattitaaatgcitta aatgaaaaaaataatgacaggttatactcagtgtaacctgggtataacccaagatctgctgc TATGTGAGGCACTTGGCTTTTTGTGGACCCCAAGTCAAAAAACTGAAGAGAGACAGTATTAAAT AGTCGCCAATTITTCTCTGGGATAATTTCTGTAAATTTCATGGGAAAAAATTATTGAAGAAT TTCGCCTCCAGAGTATGTATGTAACTGCTCTGTGGTTGGAAGCCTGAATGTGAATCGCT GACCACCTCTCAGGCGCCGACCAGACCCGCGCGCCGACCCCTTTCGACGACCACTGGCCCGG TCCCACGGCCCAGGCCCCGAGGACCGGGCCCCGCGGCGCCACCGTCCACCGACCCCTGGCTG

PCT/US99/20111

FIGURE 94

><subunit 1 of 1, 258 aa, 1 stop ></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA64952

TTSQAPTRPAPTTLSTTTGPAPTTPVATTVPAPTTPRTPTPDLPSSSNSSVLPTPPATEAPS $\tt MRSLPSLGGLALLCCAAAAAAAVASAASAGNVTGGGGAAGQVDASFGPGLRGEPSHPFPRATA$ SPPPEYVONCSVVGSLMVNRCNQTTGQCECRPGYQGLHCETCKEGFYLNYTSGLCQPCDCSP PTAQAPRTGPPRATVHRPLAATSPAQSPETTPLWATAGPSSTTFQAPLGPSPTTPPAAERTS ><MW: 25716, pI: 8.13, NX(S/T): 5

Signal peptide: Important features of the protein:

amino acids 1-25

N-glycosylation sites.

amino acids 30-33, 172-175, 195-198, 208-211, 235-238

EGF-like domain cysteine pattern signature. amino acids 214-226.

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FIGURE 95

GTGTTTGAGAATCCCTCAATAGGCGTGCTGGAGCTCTGGGTGCTGGCCACCAACTTCAGAGA GTGTCCACCCACCTCGCTCAGCGGCTCCCGGGGCCCAGCACCAGCTCAGAATAAAGCGATTC CCTTCTGTGAGTGCTGCGTCCCAGTAGGGATGGCGCCCACAGGGTCCTGTGACCTCGGCCA $\tt CTGGGCTTCCTGTCACAG\underline{TAG}CAGGCCCAGCTGCAGAAGGACCTCACCTGTGCTCACAAGAT$ ACAGTCTGACGGAGACAGCCAGCCAGGAGGCCATGGGGGCTCTTCACCAAGTGGAGCAGGAGC CTATECCATCATCTTCACTCAGCTGGAGTTCGGGGACGAGCCCTTCAACACCGTGGAGCTGT AGCACGGGCTGGGAGGGTGTGACCAGAGTGTCATGGACCTGATAAAGCGAAACTCCGGATGG GAACGTCGTGGGGGTGGTGACCCCTCACTCCAGAAAACAACCTGCGGAACGCTGTCCTCTC CCCTGGTACGTGCTTGCGGTGGCCTCCCGGGAAAAGGGCTTTGCCATGGAGAAGGACATGAA TCTCGGTGCCCAGGGCCCAGGCCGTGTGGTTGGGAAGACTGGACCCTGAGCAGCTTCTTGGG TGCGGCGCAGTGTAGACCTGGGAGG<u>ATG</u>GGCGGCCTGCTGCTGGCTGCTTTTCTGGCTTTGG

FIGURE 96

MGGLLLAAFLALVSVPRAQAVWLGRLDPEQLLGPWYVLAVASREKGFAMEKDMKNVVGVVVT LTPENNLRTLSSOHGLGGCDQSVMDLIKRNSGWVPENPSIGVLELWVLATNFRDYAIIFTQL EFGDEPFNTVELYSLTETASQEAMGLFTKWSRSLGFLSQ

Signal peptide: amino acids 1-20

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TIGURE 97

GAAGTCAGAGGCTGATTCTTGTAGAATTNACAGCCCTCAACGTGATGAGCTATGATAACACT ACAGA<u>TGA</u>GAAACTGCAGAGACTCACCCTGATTGAGGGGATCACAGCCCCTCCAGGCAAGGGA GAAGCCTTGGGACTCGCGGGGACAGGAGGCCACTGACACCGAGTACTCGGAGATCAAGATCC ATGAATTATGTGCAGAGTGAAAAGCACACAGGCTTTAGAGTCAAAGTATCTCAAACCTGAAT TCTGCCCGCTCCTCAGTGGGGGAAGGAGGAGCTCCAGTATGCATCCCTCAGCTTCCAGATGGT CTCAGGGGCCCCTGACTGAACCTTGGGCAGAAGACAGTCCCCCAGACCAGCCTCCCCAGCT GCCAGCAGCGGGCGTGGGAGATACGGGCATAGAGGATGCAAACGCTGTCAGGGGTTCAGCCT GTCTTCCTGTCCTTCTGCGTCATCTTCGTTGTAGTGAGGTCCTGCAGGAAGAAATCGGCAAG AGAGCAAAGCCACATCAGGAGTGACTCAGGGGGTGGTCGGGGGAGCTGGAGCCACAGCCCTC ATTCACCTGCAGAGCTCAGAACCCTCTCGGCTCTCAGCAGGTCTACCTGAACGTCTCCCTGC CAGTTGACAGCAATCCCCCTGCCAGGCTGAGCCTGAGCTGGAGAGGGCCTGACCCTGTGCCCC AAATGGCTCATCTCTGTCACTCCCAGAGGGCCAGTCTCTGCGCCCTGGTCTGTGCAGTTGATG CCGCCTCAGAACTTGACCATGACTGTCTTCCAAGGAGACGGCACAGTATCCACAGTCTTGGG GGGACACCCCCTATGATCTCCTGGATAGGGACCTCCGTGTCCCCCCTGGACCCCTCCACCAC GCACCCTGGAGTCCGGCTGCCCCCAGAATCTGACCTGCTCTGTGCCCCTGGGCCTGTGAGCAG ACATCACCGGCTCTCTGTGAATGTGACAGCCTTGACCCACAGGCCCAACATCCTCATCCCAG GATTCCACCTCCTTGGGGACCCCACATACCAAGAATTGCACCCTGAGCATCAGAGATGCCAGA CCAGGATGCTCCAGTGGCCACAAACAACCCCAGCTCGGGCAGTGTGGGAGGAGACTCGGGAACC GGCTGGATTTACCCTGGCCCAGTAGTTCATGGCTACTGGTTCCGGGAAGGGGGCCAATACAGA CCTGCTCTGGGGGAGGGGGGGGGGAGGACAAGACAAGTAAACTGCTGACGATGCAGAGTT TCACAGCCCTCAAACCCGGGGGTGCTGGAGCTGCCTTGGGTGCACCTGAGGGATGCAGCTGA AGGTGACCTTCCCTGGGGCCAGCGTGACCACGAACAAGACCGTCCATCTCAACGTGTCCTAC CCGCTCCTCGGTGCTCACCCTCATCCCACAGCCCCAGGACCATGGCACCAGCCTCACCTGTC agaagtgatgcggggagatacttctttcgtatggagaaaggaagtataaaatggaattataa CCGTGACGGTGCAGGAAGGCCTGTGTGTCCATGTGCCCTGCTCCTTCTCCTACCCCTCGCAT $\mathtt{AACAGACGTTCCCTCGCGGCCCCTGGCACCTCTAACCCCCAGAC}$

FIGURE 98

MLLLLLPLLMGRERAEGOTSKLLTMQSSVTVQEGLCVHVPCSFSYPSHGMTYPGDVVHGYWF
REGANTDQDAPVATNNPARAVMEETRDRFHLLGDPHTKNCTLSIRDARRSDAGRYFFRMEKG
SIKMNYKHHRLSVNVTALTHRENILIPGTLESGCPQNLTCSVPMACEGGTPPMISMIGTSVS
PLDFSTTRSSVLTLIPQPQDHGTSLTCQVTFPGASVTTNKTVHLNVSYPPQNLTMTVPQCDG
TVSTVLGNGSSLSLPEGOSLRLVCAVDAVDSNPPARLSLSMRGLTLCPSQPSNPGVLELPMV
HLRDAAEFTCRAQNPLGSQQVYLNVSLQSKATSGVTQGVVGGAGATALVFLSFCVIFVVVRS
CRKKSARPAAGVGDTGIEDANAVRGSASQGPLTEPMAEDSPPDQPPPASARSSVGEGELQYA
SLSFQMVKPMDSRQQEATDTEYSEIKIHR

Signal peptide:

amino acids 1-15

Transmembrane domain:

amino acids 351-370

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FIGURE 99

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FIGURE 100

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA65404
<subunit 1 of 1, 170 aa, 1 stop</pre>

<MW: 19457, pI: 9.10, NX(S/T): 0

MKTLFLGVTLGLAAALSFTLEBEDITGTWYVKAMVVDKDFPEDRRPRKVSPVKVTALGGGKL EATFTFMREDRCIQKKILMRKTEEPGKYSAYGGRKLMYLQELPRRDHYIFYCKDQHHGGLLH MGKLVGRNSDTNREALEEFKKLVQRKGLSEEDIFTELQTGSCVPEH

Important features:
Signal peptide:
amino acids 1-17

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FIGURE 101

GAAATATTGTGACTCTGGGAATGACAACACCTGGTTTGTTCTCTGTTGTATCCCCAGCCCCA CTGTCACTTAATAATCAACCTGGGGTTCGAAATCAGTGAGACCTGGATTCAAATTCTGCCTT $\mathtt{GAAAGTCTGCAAATATGTGGACTGGATCCAGGAGACGATGAAGAACAAT\underline{\mathtt{TAG}}\mathtt{ACTGGACCCA}$ CAAGGCATTATCTCCTGGGGCCAGGATCCGTGTGCGATCACCCGAAAGCCTGGTGTCTACAC **AAAAAAAAAAAAAAAAAAAAA** AAGAAACCCTAAGCCAAGACCCTCTACGAACATTCTTTGGGCCTCCTGGACTACAGGAGATG CCCACCACAGCCCATCACCCTCCATTTCCACTTGGTGTTTGGTTTCCTGTTCACTCTGTTAAT AAGGGGGCAAGGACTCCTGCCAGGGTGACTCCGGGGGGCCCTCTGGTCTGTAACCAGTCTCTT AGCCCCAGTTACGCCTGCCTCACACCTTGCGATGCGCCAACATCACCATCATTGAGCACCA TCTCCTCACGCTGTGTCACTGCTGGCACCAGCTGCCTCATTTCCGGCTGGGGCAGCACGTCC CATCATGCTGGTGAAGATGGCATCGCCAGTCTCCATCACCTGGGCTGTGCGACCCCTCACCC ACTGAGTCCTTCCCCCACCCCGGCTTCAACAACAGCCTCCCCAACAAAGACCACCGCAATGA TAGTTCACCTGGGGCAGCACCAACCTCCAGAAGGAGGAGGGCTGTGAGCAGACCCGGACAGCC GGCGACGCTCATCGCCCCAGATGGCTCCTGACAGCCCACTGCCTCAAGCCCCGCTACA TGCAAGCCTCACTCCCAGCCCTGGCAGGCAGCCCTGTTCGAGAAGACGCGGCTACTCTGTGG AGCAGCCAAGGAACCTGGGGCCGCTCCTCCCCCCCTCCAGGCCATGAGGATTCTGCAGTTAA GTTCCGCAGATGCAGAGGTTGAGGTGGCTGCGGGACTGGAAGTCATCGGGCAGAGGTCTCAC TCCTGCTTGCTCTGGCAACAGGGCTTGTAGGGGGAGAGACCAGGATCATCAAGGGGTTCGAG

(

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EIGURE 102

<subunit 1 of 1, 250 aa, 1 stop</pre> </usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA65405

<MW: 27466, pI: 8.87, NX(S/T): 4

VCASVQEGGKDSCQGDSGGPLVCNQSLQGIISWGQDFCAITRKPGVYTKVCKYVDWIQETMKNN AVRPLTLSSRCVTAGTSCLISGWGSTSSPQLRLPHTLRCANITIIEHQKCENAYPGNITDTM CLKPRYIVHLGQHNLQKEEGCEQTRTATESFPHPGFNNSLPNKDHRNDIMLVKMASPVSITW MRILQLILLALATGLVGGETRIIKGFECKPHSQPWQAALFEKTRLLCGATLIAPRWLLTAAH

Important features:

Signal peptide:

amino acids 1-18

Serine proteases, trypsin family, histidine active site. amino acids 58-63

N-glycosylation sites.

amino acids 99-102, 165-168, 181-184, 210-213

Glycosaminoglycan attachment site.

amino acids 145-148

Kringle domain proteins.

amino acids 197-209, 47-64

amino acids 199-209, 47-63, 220-243 Serine proteases, trypsin family, histidine protein

Apple domain proteins

amino acids 222-249, 189-222

102/270

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FIGURE 103

GAGCAGTGTTCTGCTGGAGCCG<u>ATG</u>CCAAAAACCATGCATTTCTTATTCAGATTCATTGTTT AAACAAAGTCACTTTTCTCCAAGTTGTATTTGCTATTTTCCCCTATGAGAAGATATTTTGA GACATTGCTATGACAGATATGTGCCCTGGAGAAAAGCGAAAAGTAGTTATACCCCCTTCATT GAACTA<u>TAG</u>CATATTIGTATTTCTACTITTTTTTTTTAGCTATTTACTGTACTTTATGTATA AGAATGACCATGATGGTGATGGCTTCATTTCTCCCAAGGAATACAATGTATACCAACACGAT AAAAGATGAGAAGCCACGTGACAAGTCATATCAGGATGCAGTTTTAGAAGATATTTTTAAGA ATGGACAATGACAGGCAGCTCTCTAAAGCCGAGATAAACCTCTACTTGCAAAGGGAATTTGA AGATTGAACTTTATGCTGTGACCAAAGGACCACGGAGCATTGAGACATTTAAACAAATAGAC TGCATACGGAAAGGAAGGCTATGCAGAAGGCCAAGATTCCACCGGATGCTACATTGATTTTTG CACAAAATGAAGGCCACCCCAAATGGTTTGTTGTTGGTGTTTGGGCAAGTCATAAAAGGCCTA ACTAAATGCCCATTATGACGGCTACCTGGCTAAAGACGGCTCGAAATTCTACTGCAGCCGGA TCTTTTATCTGTGGGGCCTTTTTACTGCTCAGAGACAAAAGAAGAAGAGGAGAGCACCGAAGAA

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FIGURE 104

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA65406

<subunit 1 of 1, 222 aa, 1 stop</pre>

<MW: 25794, pI: 6.24, NX(S/T): 1

MPKTMHFLFRFIVFFYLMGLFTAQRQKKEESTEEVKIEVLHRPENCSKTSKKGDLLNAHYDG YLAXDGSKFYCSRTQNEGHPKMFVLGVGQVIKGLDIAMTDMCPGEKRKVVIPPSFAYGKEGY AEGKIPPDATLIFEIELYAVTKGPRSIETFKQIDMDNDRQLSKAEINLYLQREFEKDEKPRD KSYQDAVLEDIFKKNDHDGDGFISPKEYNVYQHDEL

Important features:

Endoplasmic reticulum targeting sequence.

amino acids 219-222

N-glycosylation site.

amino acids 45-48

FKBP-type peptidyl-prolyl cis-trans isomerase

amino acids 87-223, 129-142

BF-hand calcium-binding domain proteins amino acids 202-214, 195-214

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FIGURE 105

CAGAAAMEGCAGGACCATTGCTTCTTCCAGGCCTCTGCTTTCTGCTGAGCCTCTTTGGAGCT GTGACTCAGAAAACCAAAACTTCCTTGTGCTAAGTGCCCCCCAAATGCTTCCTGTGTCAATAA CACTCACTGCAACCAAAACTTCCTGTGTGTAACTTCTGGGCAGAAACTATTCACATTCC CCTTGGAGAAACCAACACTGGATATACTTCTGGATCTGGGCAGAAACTATTCACATTCC CCTTGGAGAAACTAACCCCAGGCATGGTGGTCGCCGCCTGAATCCCAGTTCTTCGGAAAC CCAAGGCAGGTGGATCACCCTGAGGTCAGAGCTTGAACCAGGCCTGGCCAACATAGTGAAAC CCCGTGTCTCTACAAAATACAAAATCAGCCGGGCGTGGTGGTGCATGCCAGTTGCAATCCCAGT TACTCGGGAGGCTGAGGCAGAAATCGCTTGAACTCAGGAGGCAGAAGTTGCAGTGAAACCC AGATCCTGCCATTGCACTCCAGCATGGATGACAGAAGCAAAGAACCC AGATCCTGCCATTGCACTCCAGCATGGATGACAGAAGCAAAGAACCCCAAATAAA

2

FIGURE 106

MQGPLLLPGLCFLLSLFGAVTQKTKTSCAKCPPNASCVNNTHCTCNHGYTSGSGQKLFTFPL ETCNARHGGSRL

Signal peptide: amino acids 1-18

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FIGURE 107

AATATCTCCTCCATCACTTCCCCTAGCTCCACTCTTGTTGGCCTGGGAACTTCTTGGAACTT CTGTTTCCTCCACCTCCACCCCCACCCCTTAACTTGGGTACCCCTCTGGCCCTCAGAGCACC GTCCTTCAAGGTCTGGTGTCCTGGGGGGTCTGTGGGGCCCTGTGGACAAGATGGCATCCCTGG ataaatataaatgaaggagggcaaaaaaaaaaaaa TAACTCCTGCCAGCCCTTCTAAGACCCCACGAGCGGGGTGAGAGAAGTGTGCAATAGTCTGGA AGTCTACACCTATATTTGCAAGTATGTGGACTGGATCCGGATGATCATGAGGAACAAC<u>TGA</u>C GCGGCGTCCCGGGGCAGGATGCCTGCCAGGGTGATTCTGGGGGGCCCCCTGGTGTGTGGGGGA CTCCCATGCCACCTGCCATGGTGTGTATCCCGGGAGAATCACGAGCAACATGGTGTGTGCAG ATCACCAACCACCCACGGAACCCATTCCCGGATCTGCTCCAGTGCCTCAACCTCTCCATCGT CCCTGCCCCTGCCCAATGACTGTGCAACCGCTGGCACCGAGTGCCACGTCTCAGGCTGGGGC CGAGCACGACCTCCGGCTGCGGCTGCGCCTGCCCGTCCGCGTAACCAGCAGCGTTCAAC CAGATCCGGCACAGCGGCTTCTCTGTGACCCCATCCCGGCTACCTGGGAGCCTCGACGAGCCA CAGCCTGCGCTGCGGGGGTGTCCTTATTGACCACAGGTGGGTCCTCACAGGGGCTCACTGCA TTCAATGGCACTGAGTGTGGGCGTAACTCACAGCCGTGGCAGGTGGGGGCTGTTTGAGGGCAC GGCTCAGCATCTTTTGCTCCTGTGTGTTCTTGGGCTCAGCCAGGCAGCCACACCGAAGATT AGGGAAAGGGTGACCTCTCAGATTCCCCCTTTTCCCCCAGACTTTGGAAGTGACCCACC<u>ATG</u>G CAAGCAGGTCATCCCCTTGGTGACCTTCAAAGAGAAGCAGAGAGGGCAGAGGTGGGGGGCAC

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FIGURE 108

MGLSIFILLCVLGLSQAATPKIFNGTECGRNSQPWQVGLFEGTSLRCGGVLIDHRWVLTAAH
CSGSRYWVRLGEHSLSQLDWTEQIRHSGFSVTHPGYLGASTSHEHDLRLLRLRLPVRVTSSV
QPLPLPNDCATAGTECHVSGWGITNHPRNPFPDLLQCLNLSIVSHATCHGVYPGRITSNWVC
AGGVPGQDACQGDSGGPLVCGGVLQGLVSWGSVGPCGQDGIPGVYTYICKYVDWIRMINNNN

Signal peptide: amino acids 1-17

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FIGURE 109

FIGURE 110

msgelsnrfoggkafgllkaroerrlabinreflcdokysdeenlþekltafkekymefdln negeidlmslkrmmeklgvþkthlemkknisevtggvsdtisyrdfvnmmlgkrsavlklvm mfegkanessþkpvgppþerdiaslþ

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FIGURE 111A

ACTGCAGTCTTCGGTGGCTGTCGGAGTGGGTGAAGGCGGGGTACAAGGAGCCTGGCATCGCC CTGGAAGGAAACCACCTAACAGCCGTGCCCAGAGAGCTGTCCGCCCTCCGACACCTGACGCT GTCCACCATAAACCTCCTGTCCAACCCCTTCAACTGCAACTGCCACCTGGCCTGGCTCGGCA GTAACTTGATCAGCTGTGTGAGTAATGACACCTTTGCCGGCCTGAGTTCGGTGAGACTGCTG GGAGACCGTGCACGGGCGCCTCTTCCGTGGCCTCAGTGGCCTCAAAACCTTGATGCTGAGGA CGAGAGGGAGCTTTCGATGGAGCAGCCAGCGTGCAGGAGCTGATGCTGACAGGGAACCAGCT TCTTCAAGAAGTTGCCCAACCTGCGGAAAATAAATCTGAGTAACAATAAGATCAAGGAGGTG TGAATATGTCACCGACCTGCGACTGAATGACAATGAGGTATCTGTTCTGGAGGCCCACTGGCA ACTCGCCAACAAGCGCATCAGCCAGATCAAGAGCAAGAAGTTCCGCTGCTCAGGCTCCGAGG CCATCCAGACACTCCACTTAGCCCAAAAACCCATTTGTGTGCGACTGCCACTTGAAGTGGCTG GCATGGCTCCTGTGCATTTGAGGGGCTTCAACGTGGCGGATGTGCAGAAGAAGAAGGACTACGTG GAAGAACCTGCAACTGGACAACAACCACATCAGCTGCATTGAAGATGGAGCCTTCCGAGCGC CTCGGGGCATCCCCCGCAACGCTGAGCGCCTTGACCTGGACAGAAATAATATCACCAGGATC CACCAAGIGIACCIGCIGCCAGCGIGGACIGCCACGGGCIGGGCICCGCGCGGITIC GGAGCGGGGCCTGCACACCATGGCCCCCCGGTGGGCAGGGTCGGCGCCGCCGTGCGCGCC CGCTGCAGTAGCCCTGAGCCCATGGCTGACAGGCTCCTGCTCACCACCCCAACCCACCGCTT GGGCTGCGGTCCCTGCGAGTGCTAACCCTCCATGGCAATGACATTTCCAGCGTTCCTGAAGG ACCTOTOCACTOTGATOCTGAGCTACAACCGGCTGAGGTGCATCCCCGTCCACGCCTTCAAC TATTGACCTGAGCAACAACAGCATCAGCATGCTGACCAATTACACCTTCAGTAACATGTCTC GCAGCAACAAGGGGCTCCGCGCCCTCCCCAGAGGCATGCCCAAGGATGTGACCGAGCTGTAC TAGCTGCCAGCTGAGCCCGCGCGCGCGGAGCAGTGCACCTGTATGGAGACAGTGGTGCGAT AAGGAGATTCCCATCCAGGATGTGGCCATCCAGGACTTCACCTGTGATGGCAACGAGGAGAG TCCCTCTATGACAATCGGATCACCACCATCACCCCTGGGGCCTTCACCACGCTTGTCTCCCT TGTGAGGGCACGATTGTGGACTGCTCCAACCAGAAGCTGGTCCGCATCCCAAGCCACCTCCC ATTACCGCAGCAGGTTCAGCAGCGAGTGCTTCATGGACCTCGTGTGCCCCCGAGAAGTGTCGC GCCGACTACCTCCAGGACAACCCCATCGAGACAAGCGGGGCCCGCTGCAGCAGCCCGCGCCG CTGCACGTGCAGCAATAACATCGTGGACTGTCGAGGAAAGGGCTTGATGGAGATTCCTGCCA CCACCTGGCCTGGCTCTCGGATTGGCTGCGACAGCGACGGACAGTTGGCCAGTTCACACTCT TTCAACCACATGCCGAAGATCCGAACTCTGCGCCTCCACTCCAACCACCTCTACTGCGACTG GATTTGAGTGAAAACCAGATCCAGGGGATCCCGAGGAAGGCGTTCCGCGGCATCACCGATGT CAGCGTCATCGAGAGAGGGCCCTTCCAGGACCTGAAGCAGCTAGAGCGACTGGGCCCTGAACA
AGAATAAGCTGCAAGTCCTTCCAGAATTGCTTTTCCAGAGCACGCCGAAGCTCACCAGACTA CGCCTGGCGCTGGCCTTGGCGCGAGCGTCCTGAGTGGGCCTCCAGCCGTCGCCTGCCC CGCGCTCCCCGCGCGCCTCCTCGGGCTCCACGCGTCTTGCCCCGCAGAGGGCAGCCTCCTCCA agtiggttgaggaagaggcggatcgtcagtgggaaccctaggtgccagaagccatttttcctc TGCCCAGCCCCACTCGGAGCCCCCATCCTGCAATGCCAACTCCATCTCCTGCCCTTCGCC TGCGCGATTTGGAGATCCTTACCCTCAACAACAACAACATCAGTCGCATCCTGGTCACCAGC ACCAAGATGGACTTCGCTGGGCTCAAGAACCTCCGAGTCTTGCATCTGGAAGACAACCAGGT

FIGURE 111B

CATGGAAAATGTGTGGCAACTGGGACCTCATACATGTGCAAGTGTGCCGAGGGCTATGGAGG GGACTTGTGTGACAACAAGAATGACTCTGCCAATGCCTGCTCAGCCTTCAAGTGTCACCATG GGCAGTGCCACATCTCAGACCAAGGGGAGCCCTACTGCCTGTGCCAGCCCGGGTTTAGCGGC GAGCACTGGCCAACAAGAGAATCCGTGCCTGGGGACAAGTAGTCCGAGAGGTGATCCGCCCCCCA GACGGCTCCTCGTTTGTAGAAGAGGTGGAGAGACACTTAGAGTGCGGCTGCCTCGCGTGTTC GTGGGCCCCAGTGCTGCCAGCCCACCCGCAGCAAGCGGCGGAAATACGTCTTCCAGTGCACG agagaatattaagtatattgtanaataaa.caaaaaatagacttaaaaaaaaaaaaaaaaaa atgteggaccccctegtgattcagcatgaaggaaatgaagctggagaggaaggtaaagaaga CTAAGCCCCTGCCCGCCTGCCTGCCACCTCTCGGACTCCAGCTTGATGGAGTTGGGACAGCC GAAAGGTTATGCATCATGTGCCACAGCCTCCAAGGTGCCCATCATGGAATGTCGTGGGGGGCT GCTGGACCGGCCCACTCTGCGACCAGGAGGCCCGGGACCCCTGCCTCGGCCACAGATGCCAC GTGCAAGCACGGCCTGTGCCGCTCCGTGGAGAAGGACAGCGTGGTGTGCGAGTGCCGCCCAG GACTTCAAGGCCCTCCCACCACAGTCCCTGGGGGTGTCACCAGGCTGCAAGTCCTGCACCGT ACCGGCCTCTAGGCGGCTTCCACGGATGCATCCATGAGGTGCGCATCAACAACGAGCTGCAG CCCCTCTACCTTGGAGGCATCCCCACCTCCACCGGCCTCTCCGCCTTGCGCCAGGGCACGG ATGATGGGCAGTTTCACAGTGTGGAGCTGGTGACGCTAAACCAGACCCTGAACCTAGTAGTG GCGGCTGGTCTATGACAGCCTGAGTTCCCCTCCAACCACAGTGTACAGTGTGGAGAGACAGTGA GGCATCCTTCTCTACAAAGGAGACAATGACCCCCTGGCACTGGAGCTGTACCAGGGCCACGT CCTCCGCCAAGGTCCGACCCCAGGCCAACATCTCCCTGCAGGTGGCCACTGACAAGGACAAC AAGCTCTGTGAGACAGACAATGATGACTGTGTGGCCCACAAGTGCCGCCACGGGGGCCCAGTG AGGTGAGCTATGCGACGAGGTGATTGACCACTGTGTGCCTGAGCTGAACCTCTGTCAGCATG AGGCCAAGTGCATCCCCCTGGACAAAGGATTCAGCTGCGAGTGTGTCCCTGGCTACAGCGGG AACAATGCCACCTGCGTCGACGGGATCAACAACTACGTGTGTATCTGTCCGGCCTAACTACAC TGGGCTTTGAGGGGCAGCGGTGTGAGATCAACCCAGATGACTGTGAGGACAACGACTGCGAA GCATGGÀGGCACCTGCCACCTGAGTGACAGCCACAAGGATGGGTTCAGCTGCTCCTGCCCTC TACAGCTACAAGGGCAAGGACTGCACTGTGCCCATCAACACCTGCATCCAGAACCCCTGTG!

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QGEPYCLCQPGFSGEHCQQENPCLGQVVREVIRRQKGYASCATASKVPIMECRGGCGPQCCQ DQEARDPCLGHRCHHGKCVATGTSYMCKCAEGYGGDLCDNKNDSANACSAFKCHHGQCHISD HGCIHEVRINNELQDFKALPPQSLGVSPGCKSCTVCKHGLCRSVEKDSVVCECRPGWTGPLC VELVTLNQTLNLVVDKGTPKSLGKLQKQPAVGINSPLYLGGIPTSTGLSALRQGTDRPLGGF QANISLQVATOKDNGILLYKGDNDPLALELYQGHVRLVYDSLSSPPTTVYSVETVNDGQFHS LLQTSPCDQYECQNGAQCIVVQQEPTCRCPPGFAGPRCEKLITVNFVGKDSYVELASAKVRP DKGFSCECVPGYSGK1.CETDNDDCVAHKCRHGAQCVDTINGYTCTCPQGFSGPPCEHPPPMV CEINPDDCEDNDCENNATCVDGINNYVCICPPNYTGELCDEVIDHCVPELNLCQHBAKCIPL CTQDPVELYRCACPYSYKGKDCTVPINTCIQNPCQHGGTCHLSDSHKDGFSCSCPLGFEGQR SEWVKAGYKEPGIARCSSPEPMADRLLLTTPTHRFQCKGPVDINIVAKCNACLSSPCKNNGT SYNRLRCIPVHAFNGLRSLRVLTLHGNDISSVPEGSFNDLTSLSHLALGTNPLHCDCSLRWL ALPRGMPKDVTELYLEGNHLTAVPRELSALRHLTLIDLSNNSISMLTNYTFSNMSHLSTLIL SNDTFAGLSSVRLLSLYDNRITTITPGAFTTLVSLSTINLLSNPFNCNCHLAWLGXWLRKRR LRKINLSNNKIKEVREGAFDGAASVQELMLTGNQLETVHGRVFRGLSGLKTLMLRSNLISCV EIRLEQNSIKAIPAGAFTQYKKLKRIDISKNQISDIAPDAFQGLKSLTSLVLYGNKITEIAK TLNNNNISRILVTSFNHMPKIRTLRLHSNHLYCDCHLAWLSDWLRQRRTVGQFTLCMAPVHL PTRSKRRKYVFQCTDGSSFVEEVERHLECGCLACS IVSGNPRCQKPFFLKEIPIQDVAIQDFTCDGNEESSCQLSPRCPEQCTCMETVVRCSNKGLR SECFMDLVCPEKCRCEGTIVDCSNQKLVRIPSHLPEYVTDLRLNDNEVSVLEATGIFKKLPN AQNPFVCDCHLKWLADYLQDNPIBTSGARCSSPRRLANKRISQIKSKKFRCSGSEDYRSRFS GLFDGLVSLQLLLLNANKINCLRVNTFQDLQNLNLLSLYDNXLQTISKGLFAPLQSIQTLHL RGFNVADVQKKEYVCPAPHSEPPSCNANSTSCPSPCTCSNNTVDCRGKGLMETPANLPEGIV MAPGWAGVGAAVRARLALALALASVLSGPPAVACPTKCTCSAASVDCHGLGLRAVPRGIPRN PELLFQSTPKLTRLDLSBNQIQGIPRKAFRGITDVKNLQLDNNHISCIEDGAFRALRDLEIL aerldldrini tri txmdfagi, knlrvlhlediqvs v i ergafqdlkqlerlrlinkiklqvi

Signal peptide:

amino acids 1-27

FIGURE 113

GCCCTAGGATTTGCAGTGAATGTCCAAATGCCTGTGTCATCTTGTCCCGTTTTCCTCCCAATA AGTGGAAAAAAGGCTGTGAGGTTTCC<u>TAA</u>ACTGGAACTGGACCCAGGATGCTTTGCAGCAAC GACACAAGGAATGAACTATTGGCAAGGCTGGAAGAACATTGTGAGGGCAGAGACCTGTCCG TCAGCCTTGATCACTGATGACCTCACAGATGCAATTATCTGTGCCAGGAAAATTGTTAAAGA ACAGCTTCGCGTGGTGCAGACGCGGAAAGCTGAAGGAGAACAACCACTGCCATGTCGCCTGC CAACACCACAGCCCGACGGTCCTGGATGACGGCAGCATCGACTATGGCATCTTCCAGATCA GACAATTACTGGGGCTTCAGCCTTGGAAACTGGATCTGCATGGCATATTATGAGAGCGGCTA GCGCCGAGTCCAAAATCTACACTCGTTGCAAACTGGCAAAAATATTCTCGAGGGCTGGCCTG CCGGCAGGCTTTGAGGATGAAGGCTGCGGGGCATTCTGACCCCTCATTGGCTGCCTGGTCACAG GACTCAACTGAGAAGTCAGCCTCTGGGGCAGGCACCAGGAATCTGCCTTTTCAGTTCTGTCT GEATGCAGGACGCTCCCCTGAGCTGCCTGTCACCGACTAGGTGGAGCAGTGTTTCTTCCGCA

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FIGURE 114

MKAAGILTLIGCLVTGAESKIYTRCKLAKIFSRAGLDNYWGFSLGNWICMAYYESGYNTTAP TVLDDGSIDYGIFQINSFAWCRRGKLKENNHCHVACSALITDDLTDAIICARKIVKETQGMN YWOGWKKHCEGRDLSEWKKGCEVS

amino acids 1-19 Signal peptide:

FIGURE 115

AGTTGATTAATTTGGCTTCATAGTATAATGAGAGCAGGGCTATTGTAGTTCCCAGATTCAAT TAAATTTTGAATGATACTGTGCCTTAATTGGTTTTCATAGTTTAAGTGTGTATCATTATCAA AACCATGTCTTTTATGCTATAATCATTCCAAATTTTTGCCAGTGTTAAGTTACAAATGTGGTG CTTGAGTCTTGAATGTGAGCCACTTTCCTATATACCACACCTCCCTGTCCACTTTTCAGAAA CAGTTTTGAAACCAAAAAAGAAACCTAGAATCTAATGCAGAAGAGATCTTTTAAAAAAATAAA AGTGAAGGAAAAATTTTTCCCCTGAAGCATTTACAGAACAGCTCTACCGATATGTTACCAAAC CCATTGACCACAGTGTCACAGGGTTTCTGTGTGAGCCTGACCCGGTGCACTTCTCAGAAGCA TCTGGAAGCCATGTACATGCAGTGCCCAGTCATTGCTGTTAATTCGGGTGGACCCTTGGAGT CTCCTCCACAGCTGCACGTGTGTGCTTTACACACCAAGCAATGAGCACTTTGGCATTGTCCC AGTCCGACCTTGGCCAGTATGTGACCTTCTTGAGGTCTTTCTCAGACAAACAGAAAATCTCC TTATGACGAGAGTCCTGGAGAATGTGGAACATTATCAGGAATTGAAGAAAATGGTCCAAC CAGCTGCGTGGAAGATTGACATCCCAAGATTGGGAGAGGGTTCATCTGATCGTGGCAGGTGG CTTTGACTCAGTTGTTCCTGAAAAGCTGGATGACCTAGTCCCCAAGGGGAAAAAATTCCTGC CCACAGGCATGCCAGCTGCATCTTAGTCAACAGCCAGTTCACAGCTGCTGTTTTTAAGGAA CAAGAGAGATTCTTTTCTTAAACGACTATACAGGGCCCCAATTGACTGGATAGAGGAATACA CATTGGTTTTTGGAGAAAAGTTCAAGCTTTTTACCTTGGTGTCTGCCTGTATCCCAGTGTTC CAGGCCATTTGCATCCCACTGTCCTTGTGTTCGGAGCCAGGGCCACACCGTCCTCAGCAGTGT **TAAAAGGTGTTTATCATAAAAAAAAAAAAAAAAAAA** CATAGCGAGAGTGCTCTGTATTTTTTTAAGATAATTTGTATTTTTGCACACTGAGATATAA TCATTCCATGTTCAGCAGAGTATTTTAATTATATTTTCTCGGGATTATTGCTCTTCTGTCTA TGCTGGTA<u>TAA</u>TCAGATTGTTTTTAAGATCTCCATTAATGTCATTTTTATGGATTGTAGACC TGCTCTCCATCAACAGATACGAAAGGAAGAAAAATCTGACTTTGGCACTGGAAGCCCTAGTA ACATTCAAGTCCCTGTCTCACATAGACCCTGATGTCCTCTATCCATCTCTAAATGTCACCAG AGGCTGGCTAGACGGCGGAAGAAGATCCTATTTTACTGTCACTTCCCAGATCTGCTTCTCAC CATGTGTTAAAAACGCCAAGCTGAATATATCATGCCCCTATTAAAACTTGTACATGGCTCCC

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FIGURE 116

DLVPKGKKFLLLSINRYERKKNLTLALEALVQLRGRLTSQDWERVIILIVAGGYDERVLENVB HYQELKKMVQQSDLGQYVTFLRSFSDKQKISLLHSCTCVLYTPSNEHFGIVPLEAMYMQCPV IAVNSGGPLESIDHSVTGFLCEPDPVHFSEAIEKFIREPSLKATMGLAGRARVKEKFSPEAP RAPIDWIEEYTTGWADCILVNSQFTAAVFKETFKSLSHIDPDVLYPSLNVTSFDSVVPEKLD MPLLKLVHGSPLVFGEKFKLFTLVSACI PVFRLARRKKI LFYCHFPDLLL1KRDSFLKRLY TEQLYRYVTKLLV

amino acids 1-15 Signal peptide:

PCT/US99/20111

FIGURE 117

AAATCTATGTTGAATCCTTTTATAAACCAGTATCACTTTGTAATATAAAACACCTATTTGTAC AACAAAGTATGAACTGGTAACATCATCAAGGGAAGAAGCTTGGATCACTGTCTCAAAGAGAT GTACTTCTTAGTGTATTGGTGAAGAGACTGCACCTACTTTCTGTGGAGGGACAGGTTATTGA CACTTGGATTCTCAGGCACACAGGAGTGTCCAGAGTTGAGGTTTGCATATATGGTGACCACA ATCTCCACACAAGTTTGATCCAGATCGGTTTGATGATGAATTAGTAATGAAAACTTTTTCCT CCTAGAGAGACCCTCGTCCTTTATGCCCTTGGTGGTACTTCAGGATCCTAATACTTGGCC AACTGACTCCAGTTTCTGCCCAGCTTCAAGATATTGAAGGAAAAATTGACCGATTTATTATT AGAGAAAATTGAGCAGCTCAGATATTGTCAGCATGTGCTTTGTGAAACTGTTCGAACTGCCA GAAGTTCAAAAAAATTATATGAAGAGATAAACCAAGTTTTTGGAAATGGTCCTGTTACTCC CCAGTTGCATAATAACTGCAAAATTGTGTACCTGGGCAATCTGTTTTTTAACCACCTCTGAA CTTAGTACAAGGGAACCTTAATGACCAACAGATCCTAGAAGACAGTATGATATTTTCTCTGG TTAAGGAACATCATAAAAGAACGAAAAGGAAGTTCAGTCAACATATTTTCATTGACTC TTGATAAAAACATGACTCGGAAAAAAACAATATGAAGATGCCCTCATGCAACTGGAGTCTGTT CTTCCAGAAGAATCATGGCACAGTTTGGTCTGAGATTGGAAAAAGGCTTTCTAGATGGGTCAC ATGAAGTCTGTTACACAGATGGTAATGGGTAGTACATTTGAAGATGATCAGGAAGTCATTCG GACTGATTCTCTGAAGAGTAACTTTGCCCCTCCTAAAGCTTTCAGAAGAATTATTAGATA CAATCTGGTGGTGGCAGTGTGAGTGAAAAACCACATGAGGAAAAATTGTATGAAAAATGGTGT ATATCAATCCCAATAAGACATCGGACCCTTTTGAAACCATGCTGAAGTCATTATTAAGGTAT CTCCTTCTGGTTTGGCAGGCGCCTCGTGGTTAGTTTGGGCACTGTTGATGTACTGAAGCAGC GTGAATAGTGGAAGTTTGCATGAGTTCCTGGTTAATTTGCATGAGAGATATGGGCCTGTGGI AAGCTGCAGGAATTCCAGGGATTACTCCAACTGAAGAAAAAGATGGTAATCTTCCAGATATT CGCCGTTACCTTCTTGCTGGCGTTGGTGGGAGCCGTGCTCTACCTCTATCCGGCTTCCAGAC GACTACGCCGATCCGAGACGTSGCTCCCTGGGCGGCAGAACCATGTTGGACTTCGCGATCTT at<u>taa</u>aattttatacatttaaaatcattgttaaattgattgaggaaaacaaccatttaaaa

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EIGURE 118

MLDPAIFAVIFLIALVGAVLYLYPASRQAAGIPGITPTBEKDGNLPDIVNSGSLHEFLVNLH
ERYGPVVSFWFGRRLVVSLGTVDVLKQHINPNKTSDPFETMLKSLLRYQSGGGSVSENHWRK
KLYENGVTDSLKSNFALLLKLSEELLDKWLSYPETQHVPLSQHMLGFAMKSVTQMVMGSTFE
DDQEVIRFQKNHGTVWSSIGKGFLDGSLDKXMTRKKQYEDALMQLESVLRNIIKERKGRNFS
QHIFIDSLVQGNLNDQQILEDSMIFSLASCIITAKLCTWAICFLTTSBEVQKKLYEBINQVF
GNGPVTPEKIBQLRYCQHVLCETVRTAKLTPVSAQLQDIEGKIDRFIIPRETLVLYALGVVL
QDPNTWPSPHKFDPDRFDDELVMKTPSSLGFSGTQECPELRFAYMVTTVLLSVLVKRLHLLS
VEGQVIETKYELVTSSREEAMITVSKRY

Signal peptide:

amino acids 1-18

Transmembrane domain: amino acids 271-290

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FIGURE 119

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FIGURE 120

MGRVSGLVPSRFLITLLAHLVVVITLFWSRDSNIQACLFLTFTPEEYDXQDIQLVAALSVTLG LFAVELAGFLSGVSMFNSTQSLISIGAHCSASVALSFFIFERWECTTYWYIFVFCSALPAVT EMALFVTVFGLKKKPF

Transmembrane domain: amino acids 12-28 (type II), 51-66, 107-124

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FIGURE 121

TECCGGACCCTGCCGCCCTGCCACTANGTCCCACTCTATGCTGCTTGCTGCCTTGCACCTTCTCCC
CCAGCCTCCTTCGACTCCGACCTANGTCCACACTATGCTGCTGCTGCAGCCCCATA
GTGCCCCGGAACGAGTGGAAGGCCCTGGAACAGACAGACCCGGCCTGCAGCCCTA
GTGCCCCGGAACGATGGAAGGCCCTGGAACACCCCAGCACCTGCAGCCTA
ACGCTANTGTGGTGATCCCACACGGCGGGCAGCAGCTGCAACACCCCGGCCTCGTGCCAGC
AGCAGGCCCGGAATGTGCAGCACACGGCGGGCAGCTGGAACTTCACGGGTGC
CACCTCCTGATTGGAAACACGCCATTATCGAAGGCCTTCATGGGCAACTTACATGG
ATCGGGTTCCTTATGGAACCCCCATGTCCATTGGCATCTACTTGGCATCTCACTGGCTTCCAGGGTGCTCCAGGTTGCCCCCACTCAGGTCCCACTCCAGGTTCCAAGGACACCTACACTTC
CCAGGGAGCCCCAACCCCCAACTATGTGCTCCAAAGGACACCTACCGGGTTCCCCCTTCCCAGGCAACTACACTCTC
CCAGGCAACCAACCCCCATTCCTACCAGAATTGGCCACCTACCACCTTCTCCCA
ATAAAAGATGTAGCTC
ATAAAAGATGTAGCTC

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FIGURE 122

MSRRSMLLAWALPSILRLGAAQETEDPACCSPIVPRNEWKALASECAQHLSLPLRYVVVSHT AGSSCNTFASCQQQARNVQHYHMKTLGWCDVGYNFLIGEDGLVYEGRGWNFTGAHSGHLWNP MSIGISFMGNYMDRVPTPQAIRAAQGILACGVAQGALRSNYVLKGHRDVQRTLSPGNQLYHL IQNNPHYRSP

Signal peptide: amino acids 1-20

KTUKE 123

GAAACCGCTGATTGCTGACTTTTGTGTGAAGAATCGTGTTCTTGGAGCAGGAAATAAAGCTT GCATGTGCTGGATCTGTTCTGTGTGTGTGTGGGTGGGGGGAGGGGAAGTCTTGT CGGATCTGGATGGCGCCCCCCCTCTCAGCAGCGGGCACGGGTGGGGGCGGGGCCGGGGCCGCAGA CATCCATGTCCCGGAGAGGGGTCCCTCAACAGTCAGCCTCACCTGTCAGACCGGGGTTCTCC ACAGCCCATCCGCGTGCTGTGTGTCCCTCTTCCACCCCAACCCCTGCTGGCTCCTCTGGGAG GCTGATGGCACACCCATCCTTAAGCTAAGACAGGACGATTGTGGTCCTCCCACACTAAGGCC CAGCCAGGCCACCCCTTTCCAAAATTCCCTCTTCTGCCAGTACTCCCCCCTGTACCACCCATT GCCCCGGGGCA GCATGAGGCTGAAGTGGCAACCCTGGGGTCTTTGATGTCTTGACAGATTGACCATCTGTCTC CAGAGGAGCTCTCCAGCCTGCCTAGTGGGCGCCCTGAGCCCCTTGTCGTGTGCTGAGCATG TCAACTTAGGATGGATGGCTGAGAGGGCTTCCTAGGAGCCAGTCAGCAGGGTGGGGTGGGGC CTTGCCATCCTGAGGAAAGATAGCAACAGGGAGGGGGGAGATTTCATCAGTGTGGACAGCCTG TGTGGGCAGGCCGATCAGTGTGGCCCCAGATCAAGTCATGGGAGGAAGCTAAGCCCTTGGTT CTCTGTGCAGCCTCACAGGGCTTTGCCACGGAGCCACAGAGAGATGCTGGGTCCCCGAGGCC CTGGTCCCAACCTGAAGCTGTGGAGTGACTAGATCACAGGAGCACTGGAGGAGGAGTGGGCT ACGAGGAGATGCCAAGTGGGGCCAGGGCCAAGTCTCAAGTGGCAGAGAAAAGGGTCCCAAGTG TGGG<u>TGA</u>CCCGGGGCAGGCCACAGAGGCCAGGCCAGGGCTGGAAGGACAGGCCTGCCCATGC CGGCTGGTCCAGAAGGTGTGCCCAGATTACAACTACCATAGTGATACCCCCTACTACCCATC GGAGCTGCTCCAGCCCTTCAAAGTCGTCTGTGTCTACATCGCCTTCTACAGCACGGACTAT GCTTTGCACCCACGACCCAGCCAAGATCTGCTCCCGAGACCACGCTCAGAGCTCAGCCACCT GCCTCCAAAATCTTCAACTGCCGGATGGAGTGGGAGAAGGTAGAACGGGGCCGCCCGGACCTC TCGTGCCCCCAGTAAAGCTGTAGAGTTCCACCAGGAACAGCAGATCTTCATCGAAGCCAAG TGGGACCTTCAGCGTCCACTTCCAACACAATGCCACAGGCCAGGGAAAACATCTCCATCAGCC TCCAACATCAAGACGGTGGCCCTGAACCTGCTCGTCACAGGGAAGATTGTGGAACCATGGCAA CGAACCACAGCCCCCACCCTCAGCCAAGGTGAAGAAATCTTTGGCTGGGGCGACTTCTAC CCTAGGGCTGCTGGCCTGGGGGAGGCTTGGGGCATTCTTGGGCAGCCCCCAACCGCC CGGGTGCCTCGGAAGCGGGGCCACATCTCACCTAAGTCCCGCCCCATGGCCAATTCCACTCT ATGATGGTCCTCCCGGCTCAGAGGACCCTGAGCGTGATGACCACGAGGGCCAGCCCGGGCCC GACTCGCTGCTTCGTGTTCCTGGTGCAGGGTAGCCTCTATCTGGTCATCTGTGGCCAGG

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FIGURE 124

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA66521
><submit 1 of 1 oso == 1 stor</pre>

><subunit 1 of 1, 252 aa, 1 stop

><MM: 28127, p1: 8.91, nX(s/T): 5

MQLTRCCFVFLVQGSLYLVICGQDDGPPGSEDPERDDHEGQPRPRVPRKRGHISPKSRPMAN
STLLGLLAPPGEAWGILGOPPNRPNHSPPPSAKVKKIFGWGDFYSNIKTVALNLLVTGKIVD
HGNGTFSVHFQHNATGQGNISISLVPPSKAVEFHQEQQIFIEAKASKIFNCRMEWEKVERGR
RTSLCTHDPAKICSRDHAQSSATWSCSQPFKVVCVYIAFYSTDYRLVQKVCPDYNYHSDTPY
VPGC</pre>

Important features of the protein:

Signal peptide:

amino acids 1-14

N-glycosylation sites.

amino acids 62-65, 127-130, 137-140, 143-146

2-oxo acid dehydrogenases acyltransferase amino acids 61-71

FIGURE 125

TACAGATGTGGAATTTTATTTGTTTAGTTTTAAAAGACTGGCAACCAGGTCTAAGGATTAGA
AAACTCTAAAGTTCTGACTTCAATCAACGGTTAGTGTGTATACTGCCAAAGAACTGTATACTG GCGGTGCGGAGCACCAACCACGAGCCATCCGAGATGAGCAACAAGACGCGCATCATTTACTT GCTCCTCTTCCTCCCCGCTGGGGATATCGGTCCGGGCGAACTCCAAGGTCGCCTTCTCG GGCAGGGCTGATTCTTGGGCGGAGGAGTAGGGTAAAGGGTTCTGCATGAGCTCCTTAAAG TATATTTATCTGTTTAGCTAATATTAAATTCAAATATCCCATATCTAAATTTAGTGCAATAI TTTTCAAGGCTTCTGTTGTATTTGAAGTATCATCTGGTTTTGCCTTTAACTCTTTAAATTGTA ACAGTCAAAAGCTGTCTGCAAGACTTATTCTGAATTTCATTTCCTGGGATTACTGAATTAGT CATCGTGCTGGAGGGCAAGTGTCTGGTGGTGTGCGACTCGAACCCGGCCACGGACTCCAAGG GCCGTGCTGGTGCTCACGCTGCCGGGGCTGCCCGTCTGGGCACAGAACGACACGGAGCC GCCTGCGGCTGCCCACACGGCTCACC<u>AT</u>GGGCTCCGGGCGCCGGGCGCTGTCCGCGGTGCCG CATCTTCCCGAGCACCGGGATCCCGGGGGTAGGAGGCGACGCGGGGGAGCACCAGCGCCAGCC TGGTGGAAGTGTGCGCGCCGCCGCCGCCGTCGTCGCTGCAGCGCTGTCGACCTAGCCGCTAG gacaaaggtaacagagccagcgagagagctcgaggggagactttgacttcaagccacagaat GTGAATGTGAGGGTTTGATGACTTTCAGATGTCTAGGAACCAGAGTGGGTGCAGGGGCCCCA TTAATATATGTTAAAAAAA

> WO 00/12708 PCT/US99/20111

FIGURE 126

GWQYSTFSGFLVFPL HVIKVYQSQTIQVNLMLNGKPVISAFAGDKDVTREAATNGVLLYLDKEDKVYLKLEKGNLVG SVRAANSKVAFSAVRSTNHEPSEMSNKTRIIYFDQILVNVGNFFTLESVFVAPRKGIYSFSF MGSGRRALSAVPAVLLVLTLPGLPVWAQNDTEPIVLEGKCLVVCDSNPATDSKGSSSSPLGI

amino acids 1-27 Signal peptide:

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FIGURE 127

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FIGURE 128

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA66658
><subunit 1 of 1, 257 aa, 1 stop</pre>

><MW: 28472, pI: 9.33, NX(S/T): 0

MTAAVFFGCAFIAFGPALALYVFTIAIEPLRIIFLIAGAFFWLVSLLISSLUWFMARVIIDN KDGPTQKYLLIFGÁFVSVYIQEMFRFAYYKLLKKASEGLKSINPGETAPSWRLLAYVSGLGFGIMSGVFSFVNTLSDSLGPGTVGIHGDSPQFFLYSAFMTLVIILLHVFWGIVFFDGCEKKKWGILLIVLHTLLVSAQTFISSYYGINLASAFIILVLMGTWAFLAAGGSCRSLKLCLLCQDKNFLLVNQRSR

Important features of the protein:

Signal peptide:

amino acids 1-19

Transmembrane domains:

amino acids 32-51, 119-138, 152-169, 216-235

Glycosaminoglycan attachment site. amino acids 120-123

Sodium:neurotransmitter symporter family protein amino acids 31-65

FIGURE 129

GGERANCEACCAGCGECCACACCATICCLTICCOCCCTECCOGACCAMMINISTICACIONET TO CONTROL TRANSPORDED TO C

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FIGURE 130

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA66659

><subunit 1 of 1, 832 aa, 1 stop ><MW: 94454, pI: 6.94, NX(S/T); 12

MFALGLPPLUTLIVASVESHLGULGPKNVSQKDAEFERTYVDEVNSELUNIYTFNHTTVTRNRT
EGVRVSVNVLNKQKGAPLLFVVRQKEAVVSFQVPLILRGMFORKYLYQKVERTLCQPPTKNE
SEIQFFYVDVSTILSPUNTTYQLRVSRMDFVLRTGEQFSFNTTAAQEQYFKVEFPEGVDSVI
VKVTSNKAFFCSVISIQDVLCPVYDLDNNVAFIGMYQTYYTKKAAITVQRKDFPSNSFYVVVV
VKTEDQACGGSLPFYPFAEDE?VDQGHRQKTLSVLVSQAVTSEAYVSGMLFCLGIFLSFYLL
TVLLACWENWRQKKKTLLVAIDRACPESGHPRVLADSFPGSSPYEGYNYGSFENVSGSTDGL
VDSAGTGDLSYGYOGRSFEPVGTRPRVDSMSSVEEDDYDTLTDIDSDKNVIRTKQYLYVADL
ARKDKRVLRKKYQIYFMNIATIAVFYALPVVQLVITYQTVVNVTGNQDICYYNFLCAHPLGN
LSACYHVCPNYTNFQFDTSFMYNIAGLCMLKLYQKRHDDINAGAYSAYACLAIVIPFS
VLGVVFGKGNTAFWIVFSIIHIIATLLLSTQLYYMGRWKLDSGIFRRILHVLYTDCIRQCSG
PLYVDRWVLLVMGNVINWSLAAYGLIMRPNDFASYLLAIGICNLLLYFAFYIIMKLRSGERI
KLIFILCIVCTSVVWGFALFFFFGGLSTWQKTPAESREHNRDCILLDFFDDHDIWHFLSSIA
MFGSFLVLLTLDDDLDTVQRDKIYYF

Important features of the protein:

Signal peptide:

amino acids 1-18

Transmembrane domains:

amino acids 292-317, 451-470, 501-520, 607-627, 751-770

Leucine zipper pattern.

amino acids 497-518

N-glycosylation sites.

amino acids 27-30, 54-57, 60-63, 123-126, 141-144, 165-168, 364-367, 476-479, 496-499, 572-575, 603-606, 699-702

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FIGURE 131

ACTGTC<u>TGA</u>ATGGCCCAGGCAGCTCTAGCTGGGAGCTTGGCCTCTGGCTCCATCTGAGTCCC TICACCCTIGGTCCCAACCCCACGGTGCAACGGGATTGGCGCCCCCAGACTCTCAATGGTTC CCATGCCTACCTCACCTTGGCCCTGCATTGGGTGGAAGCCACGTGAACACATAATCCCCCGTGG GCTTGATCGTGAGTGGACCCAGCAAGGACCCCGATCTGGCCAGTGGGCACGGTCCCTACAGC GCCCAGTCCCTGCAGGGCGCCCAGCCTGGGGACACCTACACGGTGCTTGTGGAGGCCCAGGA GTGATGCCACCCCCAAGTTGGACCAGGAGAGCTACGAGGCCAGTGTCCCCATCAGTGCCCC GAACCTCAGTTATGAGGCAGCTCCAAGTCATGAGGTGGTGGTGGTGGTGCAGAGTGTGGCGA GAAGTCGAAGTCGCAGTCACAGATATCAATGATCACGCCCCTGAGTTCATCACTTCCCAGAT CACGTTGTGTATCAGCTCCTGAGCCCTGAGCCTGAGGATGGGGTAGAGGGGAGAGAGCCTTCCA
GGTGGACCCCACTTCAGGCAGTGTGACGCTGGGGGTGCTCCCACTCCGAGCAGCAGGACA TGACAACGTGCCTATCTGCCCTCCCCGTGACCCCACAGTCAGCATCCCTGAGCTCCAGTCCACCAGGTACTGAAGTGCCCCGGCTCCCCCAATTCC TTTATGGACTGCCCATGGGAGTGCTCCAAATGTCAGGGTGTTTGCCCAATAATAAAGCCCCCA CTGCCCTGGGGTGGAGGCACCATCACCATCACCAGGCATGTCTGCAGAGCCTGGACACCAAC CTGGGAGAGAGCCCCAGCACCCAAGATCCAGCAGGGACAGGACAGAGTAGAAGCCCCCTCCAT ACTGGACCATGTCAAGGAAGAAGGACCCGGATCAACCAGCAGACAGCGTGCCCCTGAAGGCG gtggaggggcagtgcatgcgcaaggtgggccgcatgaagggcatgcccacgaagctgtcggc TGGTCAGCCACAATGCCCAGATGTGGCAGCTCCTGGTTCGAGTGATCGTGTGTCGCTGCAAC TACAGCCCTGACTCTTGCCCCTGTGCCCTCCCAATACCTCTGCACACCCCGCCAAGACCATG CCCTAGTCAATGACTCAGAGGGCTGGCTCTGCATTGAGAAATTCTCCGGGGAGGTGCACACC AGCTGGTGGGGCCAGGCCCAGGCCCTGGAGCCACCGCCACGGTGACTGTGCTAGTGGAGAGA GAAGGGACTTTTGGCCTGGATTGGGAGCCAGACTCTGGGCATGTTAGACTCAGACTCTGCAA TTGATGCTGACCTCGAGCCCGCCTTCCGCCTCATGGATTTTTGCCATTGAGAGGGGGAGACACA TGGGCCTATAAGCCTCCCTGAGGATGTGGAGCCCGGGACTCTGGTGGCCATGCTAACAGCCA GAGAATCTCAAAGTCCTATACCCGCACCACATGGCCCAGGTACACTGGAGTGGGGGTGATGT CCACCGTGGAAGTCTCCATCATAGAGAGCACCTGGGTGTCCCTAGAGCCTATCCACCTGGCA CTACCAGCTGTTGGTACAGGTCAAGGACATGGGTGACCAGGCCTCAGGCCACCAGGCCACTG CTGGGGGCTCTGGCCCTCAGCCCCAAGGGGAGCACCAGCCTTGACCACGCCCTGGAGAGGAC CTTCCTTCCTTGAGGCTTCAGACCGGGATGAGCCAGGCACAGCCAACTCGGATCTTCGAT CCCCATITCTCTCAAGCCATCTACAGAGCTCGGCTGAGCCGGGGTACCAGGCCTGGCATCCC GGCCCTGGACCGAGAGCAGCAGCAGAGTACCAGCTACAGGTCACCCTGGAGATGCAGGATG CCAGCCTGCAGAGCTGTCTGTGGAAGTTCCAGAAAACTATGGTGGAAATTTCCCTTTATACC agtiggscatccttgtaggcaccctggtagcaataggaatcttcctcatcctcattttcaccc AGCCGGCTCTTTCCTGCTGACCATCCAGCCCTCCGACCCCATCAGCCGAACCCTCAGGTTCT TCCTGCTTCTGGTGCTGGCCATGGACCTGGCAGGCGCAGAGGGTGGCTTCAGCAGCACGTGT ACGTGACCAGAGAGCTGGACAGAGAAGCCCAGGCTGAGTACCTGCTCCAGGTGCGGGCTCAG GCACTATCACCTGGAGAGCCATCCCCCGGGACCCTTTGAAGTGAATGCAGAGGGAAACCTCT TCCACATCCTGAGCCAGGCTCCAGCCCAGCCTTCCCCAGACATGTTCCAGCTGGAGCCTCGG GACATGTCTTGTGGGGTCCACAGCCTGTGCCTTGTGCACGTGAAGGATGAGAATGACCAGGTG GGCAAGGCAACTGAGGGGCCCATTTGCTATGGATCCAGATTCTGGCTTCCTGCTGGTGACCAG TGACCAAGTTGCCCCCGCGGGGGGGGCTGAAGGCCAGATCGTGCTGTCAGGGGACTCA ACCATGGTCCCTGCCTGGCTGTGGCTTGTGTTTGTGTCTCCGTCCCAAGGCTCTCCCCAAGGC TCTCTTCTTGCTTGGCAGCTGGACCAAGGGAGCCAGTCTTGGGCGCTGGAGGGCCTGTCCTG

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FIGURE 132

MVPAMLMILLCUSVPQALPKAQPAELSVEVPENYGGNFPLYLTKLPLPREGAEGQIVLSGDSG
KATEGPFAMDPDSGFLLVTRALDREEGAEYQLQVTLEMQDGHVLMGPQPULVHVKDENDQVP
HFSQAIYRARLSRGTRPGIPFLFLEASDRDERGTANSDLRFHILSQAPAQPSPDMFQLEPRL
GALALSPKGSTSLDHALERTYQLLVQVKDMGDQASGHQATATVEVSI I ESTWYSLEPIHLAE
NLKVLYPHHMAQVHWSGGDVHYHLESHPPGPFEVNAEGNLYVTRELDREAQAFYLLQVRAQN
SHGEDYAAPLELHVLVNDENDNVP I CPPRDPTVS I PELSPFGTEVTRLSAEDADAPGSPNSH
VVYQLLSPEEPEDGVEGRAFQVDFTSGSVTLGVLPLRAGQNILLLLVLAMDLAGAEGGFSSTCE
VEVAVTD INDHAPEFITSQIGP I SLPEDVEPGTLVAMLTAIDADLEDAFRLMDFA I ERGDTE
GTFGLDWEPDSGHVYLLRLCKNLSYEAAPSHEVVVVQSVAKLVGPSGPGFGATATVTVLVERV
MPPPKLDQESYEASVPISAPAGSFLLTIQPSDFISRTLRFSLVNDSEGWLCIEKFSGEVHTA
QSLQGAQPGDTYTVLVEAQDTALTLAPVPSQYLCTDRQDHGLLVSGPSKDPDLASGHGPYSF
TLGPNETVGRDWRLQTLWGSHAYLTLALHWYEPREH I I PVVVSHNAQMWQLLVRV I VCRCKV
EGQCMRKYGRMXGMPTKLSAVGILVGTLVAIGIFLILIFTHWTMSRKKDPDQFADSVPLKATV
EGCCMRKYGRMXGMPTKLSAVGILVGTLVAIGIFLILIFTHWTMSRKKDPDQFADSVPLKATV

Signal peptide:

amino acids 1-18

Transmembrane domain:

amino acids 762-784

FIGURE 133

GICICICCCICCICCICCICTITITITITITITITIAGACAGAGITTIGCICITGTIGCC
CAGGCIGGAGIGIGAATGGCICGATCITGGCICACACCACAACCICTGCCICCIGGGIICAAGCA
AIICICCIGCCICAGCCICTIGAGIAGCITGGTITATAGGCGCATGCCACCAIGCCIGGCIA AGCATCACCCCTTCCTGGGTGGCATGTCTCTCTCTCTCACCTCATTTTTAGAACCAAAGAACATC
TGAGATGATTCTCTACCCTCATCCACCTCTAGCCAAGCCAGTGACCTTGCTCTGGTGGCACT
GTGGGAGACACCACTTGTCTTTAGGTGGGTCTCAAAGATGATGTTAGAATTTCCTTTAATTTC
TCGCAGTCTTCCTGGAAAATATTTTCCTTTGAGCAGCAAATCTTGTAGGGATATCAGTGAAG CGTGTGTCCTGGCGGTGTCCCTGCAAGAACTGGTTCTGCCAGCCTGCTGGAATTTTGGTCCTG CATCATGGAGCATGTGCGGGACAACCTCTACTAGGCGATGGCTCTGCTCTGTCTACATTTAT GTACCAAGTGGGTCCCACCTGCACCACTGTCTATCCAGCTAGCGGGAGCAGCATCGACTGGG TIGTTTTTTTGCTTTTACCAAACATGTCTGTAAATCTTAACCTCCTGCCTAGGATTTGTAC TCTGTCTATTTTGTATCCTGGACCACAAGTTCCTAAGTAGAGCAAGAATTCATCAACCAGCT CTTTGCCTTTTGAACTCACTTCAAAGATCTAGGCCTCATCTTACAGGTCCTAAATCACTCAT GTGACCATCTAAATTGCAGGATGGTGAAATTATCCCCATCTGTCCTAATGGGCTTACCTCCT accaggatogcoggaogggatctgtgtcactgtacgtactgtgcccaogaaggctgggtgaa TGCCGGGCCCGTCCCTTTTTTAGGCCTGAATACAAAGTAGAAGATCACTTTCCTTCAC ACCTCAGGTGATCTGCCCTCCTTGGCCTCCCAGAGTGCTGGGATTACAGGTGTGAGCCACTG ATTTTGTGTTTTTAGTAGAGACAGGGTTTCTCCATGTTGGTCAGGCTGGTCTCAAACTCCCA TCAGAGCCCTCTGGGTTTGTGGAGCACACAGGCCTGCCCCTCTCCAGGCAGCTCCCTGGAGT TTGTACCCACACGTGCACGCACTGAGGCCATTGTTAAAGGAGCTCTTTCCTACCTGTGTGAG TTCCTCCTGCCAGCTAACCAGATCATCCCCACTGCAGAGGAGACGTGGCTGGGGCTGAAGAC CAGGAACTCGACAAGGTGGCGAGGCTTGCGGCCAAAGCTCTGGCTTCTGTGTCGGGCACTGA GGTGAAATCAGTGGTAGATTTCATCCAAAAACATGGGAATTTCAAGGGCTTCATĆCAACCTGCAGGCTACTGCTAGTCAGAGCTGCTGATGTATTCGATATTGGTACTCAGTCAAAAAGGCCCCAGATGCC GGAGCCAGCGACAACCCCTTGCTCCGAAGTGTACCATGGACCCCCACGCCAATTCGGAAGTGGA CTGGAAGCTCCTGCATTGGTGCTGACCCCAAATAGAAACTGGAACGCTAGTTTTGCAGGAAAG TGATGGATATCTGTATACTCAAACTCAAAACCGATTATGGAGGAAGACGCGGTCCCGAAATC CATCCAGCTATCACCTCCATCTTGGAGAAAATGGATATTTTCTTGTTGCCTGTGGCCAATCC AGTGGATCTCCCAGGCCACTGCAATCTGGACGGCAAGGAAGATTGTATCTGATTACCAGAGG CAGCACTGGGAAAAGGCGTGAGGCGGCCGGCCGTTTGGCTGAATGCAGGCATCCATTCCCGAG CTTACCATTCCCTGGAAGCTATTTACCACGAGATGGACAACATTGCCGCAGACTTTCCTGAC AGATGATGAAATGCAACACAATGAAGGGCAAGAACGGAGCAGTAATAACTTCAACTACGGGG GAAAAATTTTTTTGGGGACCAAGTTTTGAGGATTAATGTCAGAAATGGAGACGAGATCAGCAA agat c ccagggcttagagtacgcagtgacaattgaggacctgcaggcccttttagacaatga CCGGGGAC<u>ATG</u>AGGTGGATACTGTTCATTGGGGCCCTTATTGGGTCCAGCATCTGTGGCCAA

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FIGURE 134

MRWILFIGALIGSSICGOEKFFGDQVLRINVRNGDEISKLSQLVNSNNIKLNFWKSPSSFNR
PVDVLVPSVSLQAFKSFLRSQGLEYAVTIEDLQALLDNEDDEMQHNEGQERSSNNFNYGAYH
SLEAIYHEMDNIAADFFDLARRVKIGHSFENRFMYVLKFSTGKGVRRPAVMLNAGIHSREMI
SQATAIWTARKIVSDYQRDFAITSILEKMDIFLLFVANFDGYVYTQTQNRLWRKTRSRNFGS
SCIGADFNRWNASFAGKGASDNFCSEVYHGFHANSEVEVKSVVDFIQKHGNFKGFIDLHSY
SQLLMYFYGYSVKKAFDAEELDKVARLAAKALASVSGTEYQVGFTCFTVYFASGSSIDWAYD
NGIKFAFTFELADTGTYGFLLPANQIIFTAEETWLGLKTIMEHVRDNLY

Signal peptide: amino acids 1-16

FIGURE 135

CAAACCACATCCCTCTTTCTGTTCTGAGGGTGCATTTGACCCCAGTGGAGCTGGATTCGCTG CTAAATCCTAGGTGGGAAATGGCCTGTTAACTGATGGCACATTGCTAATGCACAAGAAATAA GATGATGATTACAAATAAAGCCACAGACGGTATTCTCTTTCTAGGGAAAAGTGGAAAATCCCCA TTCATAGTCCGATCGAAGGATGGTCCCTCTTACTTCACTGTCTCCTTCAATAGGACCTTCCT CAAAAATGCTGATTTTTCTGGAATTGCAAAGAGAGACTCCCTGCAGGTTTCTAAAGCAACCC GTGGATACAGAGCTGAACTGCTTTGTGCTGCAGATGGATTACAAGGGAGATGCCGTGGCCTT GTAGACATAATCCAAGGCCTTGACCTTCTGACGGCCATGGTTCTGGTGAATCACATTTTCTT AAATTTCTTGGGCAATGTCAAGAGGCTGTATGAAGCAGAAGTCTTTTCTACAGATTTCTCCA CCGAGTCAGAACATCTTCTTCTCCCCTGTGAGTGTCTCCACTTCCCTGGCCATGCTCTCCCT AGGTGTATTCCCTCAACACCGACTTTGCCTTCCGCCTATACCGCAGGCTGGTTTTGGAGACC CCCGGCCAATGCCCCAGTGCATACCCCCGGCCTTCCTCCACAAAGAGCACCCCTGCCTCAC GCATCTTACCTTTATGGAGTACTCTTTGCTGTTGGCCTCTGTGCTCCAATCTACTGTGTGTC CAACCATGCAAGGACAGGGCAGGAGAAGAGGAACCTGCAAAGACATATTTTGTTCCAAA<u>AT</u>G CCAGGTTAGGCACCTCTATTGCAGAATTACAATAACACATTCAATAAAACTAAAATATGAAT GGATGTTGCTGGGTTACCATATTTCCATTCCTTGGGGCTCCCAGGAATGGAAATACGCCAAC AACACCCATTAAACCCCAGTCAGTGCCCTTTTCCACAAATTCTCCCCAGGTAACTAGCTTCATG GCAGGGATGCCACTTCCAAGGCTCAATCACCAAACCATCAACAGGGACCCCAGTCACAAGCC ACAAGGCTGTGCTGGATGTCAGTGAAGAGGGCACTGAGGCCACAGCAGCTACCACCACCAAG ATTTCTGCCTCCTACAATCTGGAAACCATCCTCCCGAAGATGGGCATCCAAAATGCCTTTGA TGATAAAGTGGAGCCACTCACTCCAGAAAAAGGTGGATAGAGGTGTTCATCCCCAGATTTTCC CTTTGTCCTCCCTAGCAAGGGCAAGATGAGGCAACTGGAACAGGCCTTGTCAGCCAGAACAC TGGGCGAGCAGGTCACTGTGCAAGTCCCCATGATGCACCAGAAAGAGCAGTTCGCTTTTGGG ACCCCTCCATTGCCCAGGCGAGGATCAACAGCCATGTGAAAAAGAAGACCCAAGGGAAGGTT AAAGACCTGACCTTGAAGATGGGAAGTGCCCTCTTCGTCAAGAAGGAGCTGCAGCTGCAGGC

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EIGURE 136

MASYLYGVLFAVGLCAPIYCVSPANAPSAYPRPSSTKSTPASQVYSLNTDFAFFLYRRLVLE
TPSQNIFPSPVSVSTSLAMLSLGAHSVTKTQILQGLGFNLTHTPESAIHQGFQHLVHSLTVP
SKDLTLKMGSALFVKKELQLQANFLGNVKRLYEAEVFSTDFSNPSIAQARINSHVKKKTQGK
SKDLTLKMGSALFVKKELQLQANFLGNVKRLYEAEVFSTDFSNPSIAQARINSHVKKKTQGK
VVDIIQGLDLLTAMVLVNHIFFKAKWEKPFHLEYTRKNFPFLVGEQVTVQVPMMHQKEQFAF
GVDTELNCFVLQMDYKGDAVAFFVLPSKGKMRQLEQALSARTLIKWSHSLQKRWIEVFIPRF
SISASYNLETILPKMGIQNAFDKNADFSGIAKRDSLQVSKATHKAVLDVSSEGTEATAATTT
KFIVRSKDGPSYFTVSFNRTFLMMIINKATDGILFLGKVENPTKS

Signal peptide: amino acids 1-20

FIGURE 137

ACTGCCACCAACTCTGAGTCCAGCACAGTGTCCAGTAGGGGCAGCAGCAGCACCAACTCTGAGTCTAGCACAACTCTGAGTCAGCACAGACACAGCCACCAACTCTGACTCCAGCACAACCTCCA ACAACCTCCAGTGGGGTCAGCACAGCCACCAACTCTGAGTCCAGCACAACCTCCAGTGGGGCTAGCACAGCCACCAACT CACAACCTCCAGTGGGGCCAGCACAGCCACCAACTCTGAGTCCAGAACGACCTCCAATGGGG GTGGGGCTAGCACAGCCACCAACTCTGAGTCCAGCACAACCTCCAGTGGGGCCAGCACAGCC CCTCCAGTGGGGCCAGCACAGTCACCAACTCTGGGTCCAGTGTGACCTCCAGTGGAGCCAGC CACCAACTCTGGGTCCAGTGTGACCTCCAGTGGGGTCAGCACAGCCACCATCTCAGGGTCCA CCTTTATCTCTTCACCTTCAAGTCCCCCTTTCTCAAGAATCCTCTGTTCTTTGCCCTCTAAAG GGCTGACCGTGCTACATTGCCTGGAGGAAGCCTAAGGAACCCAGGCATCCAGCTGCCCACGC CTGAGTCCAAGATTCTTCCCAGGAACACAAAGGTAGGAGACCCACGCTCCTGGAAGGACACCAG CCAGGAGACCCCTCCCAGCTTTGTTTGAGATCCTGAAAATCTTGAAGAAGGTATTCCTCACC GGAATCATGGAGCCCCCCACAGGCCCAGGTGGAGTCCTAACTGGTTCTGGAGGAGACCAGTA CTTTAACACAGCTGTCTACCACCCTCATGGCCTCAACCATGGCCTTGGTCCAGGCCCTGGAG GCCGTGGGGCTCTTTGCTGGGCTCTTCTTCTGTGTGAGAAACAGCCTGTCCCTGAGAAACAC CTGAGTCTAGCACAGTGTCCAGTGGGATCAGCACAGTCACCAATTCTGAGTCCAGCACAACC CCAACTCTGAGTCCAGCACAGTGTCCAGTGGGGCCAGCACTGCCACCCAACTCTGAGTCCAGC TGGGGCCAACACAGCCAACTCTGAGTCCAGTACGACCTCCAGTGGGGCCAACACAGCCA TCCAGCACAGTGTCCAGTGGGATCAGCACAGTCACCAATTCTGAGTCCAGCACACCCTCCAG CAGCCACCAACTCTGACTCCAGCACAACCTCCAGTGGGGCCGGCACAGCCAACTCTGAG CTCCAGTGGGGCCAGCACAGCCACCAACTCTGAGTCCAGCACGACCTCCAGTGGGGCTAGCA ACCAACTCTGAGTCCAGCACAGTGTCCAGTAGGGCCAGCACTGCCACCAACTCTGAGTCCAG CTCTGAGTCCAGCACAACCTCCAGTGGGGCCAGCACAGCCACCAACTCTGAGTCCAGCACAC atcagcacagccaccaactctgagttcagcacagcgtccagtgggatcagcatagccaccaa GCGTGACCTCCAATGGGGTCAGCATAGTCACCAACTCTGAGTTCCATACAACCTCCAGTGGG AATGAGACTAGCACCTCTGCCAACACTGGATCCAGTGTGATCTCCAGTGGAGCCAGCACAGC AGAAAGGAAATGTTCTCCTTATGTTTTGGTCTACTATTGCATTTAGAAGCTGCAACAAATTCC TCTTGGTACATCTAGGACCCAGGCATCTTGCTTTCCAGCCACAAAGAGACAG<u>ATG</u>AAGATGC CTCTGAGATGAACTCAGTTATAGGAGAAAACCTCCATGCTGGACTCCATCTGGCATTCAAAA TTTCTTGCCTTTACCAGACACTGGAAAGAGAATACTATATTGCTCATTTAGCTAAGAAATAA TCATCGATAGCCATGGAGATGAGCGGGGGGAACAGCGGGCCC<u>TGA</u>GCAGCCCCGGAAGCAAG AGCCTGGTGGGTCCCTGGTGCCGTGGGAAATCTTCCTCATCACCCTGGTCTCGGTTGTGGCG TCCAGTGGGGCCAACAGACACCAACTCTGGGTCCAGTGTGACCTCTGCAGGCTCTGGAAC

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FIGURE 138

SEAKPGGSLVPWEIFLITLVSVVAAVGLFAGLFFCVRNSLSLRNTFNTAVYHPHGLNHGLGP ATNSESSTVSSGISTVTNSESSTTSSGANTATNSGSSVTSAGSGTAALTGMHTTSHSASTAV NTATNSESSTVSSGASTATNSESSTTSSGVSTATNSESSTTSSGASTATNSDSSTTSSEAST SNGAGTATNSESSTTSSGASTATNSDSSTVSSGASTATNSESSTTSSGASTATNSESSTTSS SSTPSSGASTVTNSGSSVTSSGASTATNSESSTVSSRASTATNSESSTLSSGASTATNSDS9 MKMQKGNVLLMFGLLLHLEAATNSNETSTSANTGSSVISSGASTATNSGSSVTSSGVSTATI GPGGNHGAPHRPRWSPNWFWRRPVSSIAMEMSGRNSGP GASTATNSDSSTTSSGAGTATNSESSTVSSGISTVTNSESSTPSSGANTATNSESSTTSSGA TTSSGASTATNSESSTTSSGASTATNSESSTVSSRASTATNSESSTTSSGASTATNSESRTT SGSSVTSNGVSIVTNSEFHTTSSGISTATNSEFSTASSGISIATNSESSTTSSGASTATNSE

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 510-532

FIGURE 139

ATGACCTGGAGGGGTTGGGGGGGACAGGTTTCTGAAATCCCTGAAGGGGGTTGTACTG TGCCCTAAACTGGCATCCGGCCTTGCTGGGAGAATAATGTCGCCGTTGTCACATCAGCTGAC GGCCTCAGTCAACACGCCTTTCATCAACCTTCCCCGCCCTGTGGAGGAGCGTCGCCAACATCA AACCATCAAAGCGGATCTTCCAGCCATCAAGGAGGGGCCACAACCACGCCGTTAGCCTCTGG AAAGGAAGTGGAGAAGCTTGGCCAAGGTGCCCACCATGCTGGCCTGGCCAGGCCGGGAAGGAGC CAGGCTGGGAAGGAAGCAGAAACTTGGCCAAGGGGTCAACCATGCTGCTGACCAGGCTGG CTGCTGGACAGGCCGGGAAGGAAGCAGACAAAGCGGTCCAAGGGTTCCACACTGGGGTCCAC CAACCATGGTATTGGACAAGCAGGAAAGGAAGCAGAGAAGCTTGGCCATGGGGTCAACAACG ATGCCGGAAGGGAAGTGGAGAAGGTTTTCAACGGACTTAGCAACATGGGGAGCCACACCGGC GCTGAGCAATGCAGAGAGAGGTGGGCAAGGCCCTGGATGGCATCAACAGTGGAATCACGC CTGTCTGGATGGGCGGCCAGCGATGACCCCCATTGAGAAGGTCATTGAAAGGGATCAACCGAGG GGATTTGTGAATAAACTTGATACACCA TGCAGAATGCTCATAATGGGGTCAACCAAGCCAGCAAGGAGGCCAACCAGCTGCTGAATGGC AAGGAGTTYGGACAAAGGCGTCCAGGGGCTCAACCACGGCATGGACAAGGTTGCCCCATGAGAT CCAGCAATATGCATCTTGCACGTCTGGTCGGCTCCTCCTTCTTCTGCTACTGGGGGCC GGGAGAGAGGATAAATAGCAGCGTGGCTTCCCTGGCTCCTCTGCATCCTTCCCGACCTTC

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FIGURE 140

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA66675

><subunit 1 of 1, 247 aa, 1 stop

><MW: 25335, pI: 7.00, NX(S/T): 0

MHLARIVGSCSLLILLGMAASDDPIEKVIEGINRGLSNAEREVGKALDGINSGITHAG
REVEKVFNGLSNMGSHTGKELDKGVQGLNHGMDKVAHEINHGIGQAGKEAEKLGHGVNNNAA
QAGKEADKAVQGFHTGVHQAGKEAEKLGQGVNHAADQAGKEVEKLGQGAHHAAGQAGKELQN
AHNGVNQASKEANQLLNGNHQSGSSSHQGGATTTFLASGASVNTPFINLPALWRSVANIMP

Important features of the protein:

Signal peptide:

amino acids 1-25

Homologous region to circumsporozoite (CS) repeats:

amino acids 35-225

FIGURE 141

GAACCCGTGTGCCCCCTTCCCACCATATCCACCCTCGCTCCATCTTTGAACTCAAACAACGAGGAAATAACTGCACCCGGGGGGCCCCCAGCCCAGTCCCCAGTCCCCATCCCCACCCTCACCCTCACCCTTCACCCTAAGGGATATCAACACTGCCC ССТОСТОВ ОБОВЕНИЕМ В МЕТОВ ОСТОВНОЕМ В МЕТОВ ОТ В МЕТО CTCCGGGTCCCCAGGGGTGCGCCGGGCCGGCCTGGCAAGGGGAAGAGAGTCAGTGGACACTCCAGGAAGAGGGGG \GCACAGGGGCCCTGAATTTATGTGGTTTTTATACATTTTTTAATAAGATGCACTTTATGTCATTTTTTAATAAA

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FIGURE 142

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA67962</pre>

><subunit 1 of 1, 837 aa, 1 stop

><MW: 92750, pI: 7.04, NX(S/T): 6

SRMLLLQPQARYQRVAVHRVFGLHHTYDVLFLGTGDGRLHKAVSVGFRVHIIEELQIFSSGQ EAEHISNYTALLLSRDGRTLYVGAREALFALSSNLSFLPGGEYQELLWGADAEKKQQCSFKG LWLRNGAPVNASASCHVLPTGDLLLVGTQQLGEFQCWSLEEGFQQLVASYCPEVVEDGVADQ QLATRPWIQDIEGASAKDLCSASSVVSPSFVPTGEKPCEQVQFQPNTVNTLACPLLSNLATR SRPDDGFPFNVLQDVFTLSPSPQDWRDTLFYGVFTSQWHRGTTEGSAVCVFTMKDVQRVFSG SLGSLQGDDDKIYFFFSETGQEFEFFENTIVSRIARICKGDEGGERVLQQRWTSFLKAQLLC FDPNFKSTALVVDGELYTGTVSSFQGNDPAISRSQSLRPTKTESSLNWLQDPAFVASAYIPE KDPQRDCQNYIKILLPLSGSHLFTCGTAAFSPMCTYINMENFTLARDEKGNVLLEDGKGRCP MLRTAMGLRSWLAAPWGALPPRPPLLLLLLLLLLLQPPPPTWALSPRISLPLGSEERPFLRF PLSIQDSFVEVSPVCPRPRVRLGSEIRDSVV KVFLKQGECASVHPKTCPVVLPPETRPLNGLGPPSTPLDHRGYQSLSDSPPGARVFTESEKR TDEGGSVPVIISTSRVSAPAGGKASWGADRSYWKEFLVMCTLFVLAVLLPVLFLLYRHRNSM PVQNLLLDTHRGLLYAASHSGVVQVPMANCSLYRSCGDCLLARDPYCAWSGSSCKHVSLYQP LYKEVNRETQQWYTVTHPVPTPRPGACITNSARERKINSSLQLPDRVLNFLKDHFLMDGQVR

Transmembrane domains:

amino acids 23-46 (type II), 718-738

FIGURE 143A

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FIGURE 143B

ТИМІТІТІКІМІТОСТІМСІВІТІТІМСІМАКНІТМАВІВІТСТІТОМСАМІТІТІВВІССКА ГОТОТІТІВВІ ВАСМАНДІВМІТІТІВВІ ВІДІМІТІТІВВІ ВІДІМІТІТІВВІ ВІДІМІТІВМІ ВІДІМІТІВМІ ВІДІМІ ВІТІМІ ВІДІМІ ВІДІ ВІДІМІ ВІДІМІ ВІДІМІ ВІДІМІ ВІЛІМІ ВІДІМІ ВІЛЬ ВІДІМІ ВІ ВІДІВ ВІДІМІ ВІ ВІВ ВІДІМІ ВІ ВІ ВІВ ВІ ВІДІМІ ВІ ВІ ВІДІМІ ВІ ВІ ВІДІМІ ВІ ВІДІВ ВІ ВІ

PCT/US99/20111

FIGURE 144

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA68836</pre>

>< subunit 1 of 1, 802 aa, 1 stop

><MW: 91812, pI: 9.52, NX(S/T): 3

MAARGRRAMLSVLLGLVLGFVLASRLVLPRASELKRAGPRRRASPEGCRSQQAAASQAGGAR
GDARGAQLMP PG5DPDGGPRDRNFLFVGVMTAQXYLQTRAVAAYRTMSKTIPGKVQFESSEG
SDTSVPIPVVPLRGVDDSYPPQXKSFMMLKYMHDHYLDKYEMFMRADDDVYIKGDRLENFLR
SLMSSEPLFLGQTGLGTTEEMGKLALEPGENFCMGGPGVIMSREVLRRMVPHIGKCLREMYT
THEDVEVGRCVRRFAGVQCVMSYEMRQLFYENYEONKKGYIRDLHNSKIHQAITLHPNKNPP
YQYRLHSYMLSRKISELRHRTIQLHREIVLMSKYSNTEIHKEDLQLGIPPSFMRFQPRQREE
ILEMEFLTGKYLYSAVDGQPPRRGMDSAQREALDDIVMQVMEMINANAKTRGRIIDFKEIQY
GYRRVNPMYGAEYILDLLLLYKXHKGKKMTVPVRRHAYLQQTFSKIQFVEHEELDAQELAKR
INQESGSLSFLSNSLKKLVPFQLPGSKSEHKEPKDKKINILIPLSGRFDMFVRFMGNFEKTC
LIPMQNVKLVVLLFNSDSNPDKAKQVELMRDYRIKFPKADMQILPVSGEPSRALALEVGSSQ
FNNESILFFCDVDLVFTTEFLQRCRANTVLGQQIYFPIIFSQYDPKIVYSGKVPSDNHFAFT
QKTGFWRNYGFGIICIYKGDLVRVGGFDVSIQGMGLEDVDLFNKVVQAGLKTFRSQEVGVVH
VHHPVFCDPNLDFXQYKMCLGSKASTYGSTQQLAEMGLEXUDPSYSKSSNNNGSVRTA

Signal peptide:

amino acids 1-23

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FIGURE 145

TTTAAGCAAACTGCATTTTTTCACAGGAGAAATAATCATATTCGTAATTTCAAAAGTTGTAT CTGCTACAGTATTCAATACATTAAAAAATATGTGTAGATCAAGGAGAGTCACAGCCTTATTA CACCAGCAACCCAGCATATAGAGAAGATATTGAAGCCTCTAAAGATCACCTAAAACGAAGCC GATGACATTTTGAAAAAATTTTAGATATTAATTCACAAGTGCAACAGGCACTTCTTAGTGA CAGGTGAAACTGCGATAGAAAAACCCCGAAGAGTTTGGAAAGCCACCCAGAGAGTTGGAATAAT CACTTAGATAAGAGCACTGGCATTGAGATCTCTACAGAATCAGAAGATGTTCCTCAGCTCT CACATGGAGACGCTTCAACTGAGAATGATGTTTTAACCAATCCTATCAGTGAAGAAACTACA CAAGTTTTAGAGAACCTAGTACGAAGTGTTCCCTCTGGGGAGCCAGGTCGTCAGAAAAATC ACGGACGACGCCTATGAAGCCCTTAGTCCTTCTAGTTGCGCTTTTGCTATGGCCTTCGTCTG ATTTTCATATGCACTABABACCTAATTTABABATABAATTTTGGTTCAGGABBBA aaaaatattttctattgtagttcaaatgtgccaacatctttatgtgtcatgtgttatgaaca AAAGTTTAT<u>TAA</u>ACAATAATATAAAAATTTTAAACCTACTTGATATTCCATAACAAAGCTGA TAGATCTAAACTCTATGAATATTTAGATATTAAATGTGTTCCACCAGAGATGAGAGAAAAAAG GTAGGACGAACAAGTAATAAAATTGATGACATCGAAACTGTTATTAACATGCTGTGTAATTC TTGCTCTAGCAGCAGCAGCAGAACATAAATTAAAAACAATGTATAAGTCCCAGTTATTGCCA TTGCCAGTTGTTACTGAATCATCTACAAGTCCATATGTTACCTCATACAAGTCACCTGTCAC TAACTCTCCAAAACATGTTTATTCTATAGCATCAAAGGGATCAAAATTTAAGGAGCTAGTTA TGCCGGCTTATCCGAGCATAACTGTGACACCTGATGAAGAGCAAAACTTGAATCATTATATA TTTCGGCCTTGAGGTTCCCAGCCTGGTGGCCCCAGGACGTTCCGGTCGCATGGCAGAGTGCT GGACAACCGTTGCTGGGTGTCCCAGGGCCTGAGGCAGGACGGTACTCCGCTGACACCTTCCC

FIGURE 146

><subunit 1 of 1, 350 aa, 1 stop ></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA68864

><MW: 39003, pI: 5.59, NX(S/T): 1

AYREDIEASKDHLKRSLALAAAAEHKLKTMYKSQLLPVGRTSNKIDDIETVINMLCNSRSKL STGIEISTESEDVPQLSGETAIEKPEEFGKHPESWNNDDILKKILDINSQVQQALLSDTSNP KPNNVSIVLHAEEPYIENBEPEPEPEPAAKQTEAPRMLPVVTESSTSPYVTSYKSPVTTLDK HVYSIASKGSKFKELVTHGDASTENDVLTNPISEETTTFPTGGFTPEIGKKKHTESTPFWSI MKPLVLLVALLLMPSSVPAYPSITVTPDEEQNLNHYIQVLENLVRSVPSGEPGREKKSNSPK YEYLDIKCVPPEMREKAATVFNTLKNMCRSRRVTALLKVY

amino acids 1-19 Signal peptide:

> WO 00/12708 PCT/US99/20111

EIGURE 147

TGAGGTTCTTCTGCCCTGAGCCCTGCAGCAGCGGCAGTCACAGCTTCCAGATGAGGGGGAAT TGGCCTGACCCTGTGGGAGTCAGAAGCCATGGCTGCCCTGAAGTGGGGAACGGAATAGACTCA CATTAGGTTTAGTTTGTGAAAAACTCCATCCAGCTAAGCGATCTTGAACAAGTCAAAACCTCC GATGGGTACAGCCTGTATGATGTGGAGATCTCCATTATAGTCCAGGAAAATGCTGGGAGCAT GATGAGGAGGCCACCTGGGAGCTGCGGGTGGCAGCACTGGGGCTCACTTCCTCTCATTTCCAT CCTGCTCCCTCTTTCCTGAGACCAGTGCAGAGGCTATGGAAGTGCGGTTCTTCAGGAATCAG GIGGCAAGTCACTGGACCGGGCAAGTTTGTCCAGGCCTTGGTGGGGGAAGGACGCCGTGTTCT GGAATATCCAIGGCTTTTGTGCTCATTTTGGTTCTCAGTTTCTACGAGCIGGTGTCAGGACA GAGGTAGGATTTTTCACTGATTCTATAAGCCCCAGCATTACCTGATACCAAAACCCAGGCAAAG TACCAMATCACCCATGGAATAGTTATTGAACACCTGCTTTGTGAGGCTCAAAGAATAAAGAG CAGGCTCCTCATTTGCTAGTCACGGACAGTGATTCCTGCCTCACAGGTGAAGATTAAAGAGA CAACGAATGTGAATCATGCTTGCAGGTTTGAGGGCACAGTGTTTTGCTAATGATGTGTTTTTA GGAAAAGGGGACTCCCATATTCATATGTCCAGTGTCCTGGGGA<u>TGA</u>GACAGAGAAGACCCTG ACTTTGTCTCCCAACAATGGGTATTGGGTCCTCAGACTGACAACAGAACATTTGTATTTCAC GAGTGTGGTGGCTTCTCAGGGTTTCCAAGCAGGGAGACATTACTGGGAGGTGGACGTGGGAC ATTGTGTTCCATCCACCTTGCTGAGCAGAGTCATGAGGTGGAATCCAAGGTATTGATAGGAG CCACAGCCAAGTGGAAAGGTCCACAAGGACAGGATTTGTCTTCAGACTCCAGAGCAAATGCA CGTGGGATATGTTGACGGAGGTATCCAGTTACTCTGCCTGTCCTCAGGCTGGTTCCCCCAGC TAAAAAACATCACTCCCTCGGACATCGGCCTGTATGGGTGCTGGTTCAGTTCCCAGATTTAC TTCCATGCTGTGGTCCACCTCTACAGAGATGGGGAAGACTGGGAATCTAAGCAGATGCCACA CAGTGTGGTTTGTCCCACAAATGCAGAGTTGGTTTAATATTTAAATATCAACCAGTGTAATT TTCTAAATAAAATTTTAACAAATTAAAACTAAAACAATATTTAAAGATGATATATAAACTACT aaaacagaagaagaaggaaaactacaggtccatatccctcattaacacagacacaaaaaa TATTATACATTTTCCCACCATAAACTCTGTTTGCTTATTCCACATTAATTTACTTTTCTCTA CTTAAAGGGCCCCACACCACAGACCCAGACACAGCCAAGGGAGAGTGCTCCCGACAGGTGGC CIGCIGACAIGICAGITTGAAGGCTTGTTGAGACCCTATATCCAGCATGCGATGTATGACGA ATTCAATCCCCATTTTATCAGCCTCCCCCCCAGCACCCCTCCTACACGAGTAGGGGTCTTCC aaaatgtagggtggtatgtgggagtgtcgggatgacgtagacagggggaagaacaatgtg ACCTCCAAATCATCCATCCACCCCTGCTGTCATCTGTTTTCATAGTGTGAGATCAACCCACA CGGCTCGAGCGGCTCGAGTGAAGAGCCTCTCCACGGCTCCTGCGCCTGAGACAGCTGGCCTG

FIGURE 148

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA68866

><subunit 1 of 1, 466 aa, 1 stop

><MW: 52279, pI: 6.16, NX(S/T): 2

MAFVLIIVLSFYELVSGQMQVTGPGKFVQALVGEDAVFSCSLFPETSAEAMEVRFFRNQFHA
VVHLYRDGEDWESKQMPQYRGRTEFVKDSIAGGRVSLRLKNITPSDIGLYGCWFSSOIYDEE
ATWELRVAALGSLPLISIVGYVDGGIQLLCLSSGWFPQFTAKWKGPQGDLSSDSRANADGY
SLYDVEISIIVQENAGSILCSIHLAEQSHEVESKVLIGETFFQPSFWRLASILLGLLCGALC
GVVMGMIIVFFKSKGKIQAELDWRRKHGQAELRDARKHAVEVTLDPETAHPKLCVSDLKTVT
HRKAFQEVPHSEKRFTRKSVVASQGFQAGRHYWEVDVGQNVGWYVGVCRDDVDRGKNNVTLS
PNNGYWVLRLTTEHLYFTFNPHFISLPPSTPFTRVGVFLDYEGGTISFFNTNDQSLIYTLLT
CQFEGLLRPYIQHAMYDEEKGTPIFCDVSWG

Signal peptide:

amino acide 1-17

Transmembrane domains:

amino acids 131-150, 235-259

FIGURE 149

AGAGACAAAAGCCTCATGGAACAGATAACATTTTTTTTGTTTTTTGGGTGTGGAGGCCATT
TTTAGAGATACAGAATTGGAGAGACTTGCAAAACAGCTAGATTTGACTGATCTCAATAAAC
TGTTTGCTTGATGCATGTATTTTCTTCCCAGCTCTGTTCCGACGGTAGACTCTTGCTTCTG
CCAGATCAACTCTGTCATCTGTGAGCAATAGTTGAAACTTTATGTACATAGAGAAATAGATA ATACAATATTACATTACAGCCTGTATTCATTTGTTGTCTAGAAGTTTTTGTCAGAATTTTGAC TTGTTGACATAAATTTGTAATGCATATATACAATTTGAAGCACTCCTTTTCTTCAGTTCCTC GTCTCCGGAGAATAATTGTCCATGAAAAATACAAAACACCCATCACATGACTATGATATTTCT GAACCCTGCCAGATGGACTGCTTCCTTTGGAGTAACAATAAAACCTTCGAAAATGAAACGGG AAGTAGAAGAGGGTGAATGGCCCTGGCAGGCTAGCCTGCAGTGGGATGGGAGTCATCGCTGT TCTCCATTAAGGGAAGAATTTGTCAAGTCTCAGGTTATCAAGTTCAGTCAACAGAAGCATGG ITATITAACATTGTTACTGAGGATGTCAACATATAACAATAAAAATATAAATCACCCA acctataataattatacaaacttcatgcaatgtacttgttctaagcaaattaaagcaaatat GGAATATTAGAAATGATCATATTCATTATGAAAGGTCAAGCAAAGACAGCAGAATACCAATC AGCTCCTCTCATTTCAGCAAATATCCATTTTCAAGGTGCAGAACAAGGAGTGGAAGAAAATA TAAGAAGAAAAAAATCCCCTACATTTTATTGGCACAGAAAAGTATTAGGTGTTTTTCCTTAGT ngaaggaaaaacagatgcatgccagggtgactctggaggaccactggttagttcagatgcta TGCAATGAACCTCAAGCTTACAATGACGCCATAACTCCTAGAATGTTATGTGCTGGCTCCTT ATGATGGTTACAGTCAAAATCATCTTCGACAAGCACAGGTGACTCTCATAGACGCTACAACT GGAGCAACCTTAATTAATGCCACATGGCTTGTGAGTGCTGCTCACTGTTYTTACAACATATAA TTGCTGCGGAACACGAAGAAGTAAAACTCTAGGTCAGAGTCTCAGGATCGTTGGTGGGACAG CTAACAATTITACAGAAATGAGCCAGAGACTTGAATCAATGGTGAAAAATGCATTTTATAAA TTACTATAGCACATTGTCATTTACAACTGACAAACTATATGCTGAGTTTGGCAGAGAGGCTT CTGGCAGTGTGCATTGGACTCACTGTTCATTATGTGAGATATAATCAAAAGAAGAACCTACAA ggaaāaģagtitgttgggaacccttgggttatcggcctcgtcatcttcatatccctgattgtc CCTTCACAGGACTCTTCATTGCTGGTTGGCA<u>ATG</u>ATGTATCGGCCAGATGTGGTGAGGGGTA

FIGURE 150

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA68871
><subunit 1 of 1, 423 aa, 1 stop
><WW: 47696, pI: 8.96, NX(S/T): 3</pre>

MMYRPDVVRARKRYCMEPWVIGLVIFISLIVLAVCIGLTVHYVRYNQKKTYNYYSTLSFTTD
KLYAEFGREASNNFTEMSORLESMVKNAFYKSPLREEFVKSOVIKFSOOKHGVLAHMLLICR
FHSTEDPETVDKIVQLVLHEKLQDAVGPPKVDPHSVKIKKINKTETDSYLNHCCGTRRSKTL
GQSLRIVGGTEVEEGEWFWQASIQWDGSHRCGATLINATMLVSAAHCFTTYKNPARWTASFG
VTIKPSKMKRGLRRIIVHEKYKHPSHDYDISLAELSSPVPYTNAVHRVCLPDASYEPQPGDV
MFVTGFGALKNDGYSONHLROAQVTLIDATTCNEPQAYNDAITPRNLCAGSLEGKTDACOGD
SGGFLVSSDARDIWYLAGIVSWGDECAKPNKPGVYTRVTALRDNITSKTGI

Transmembrane domain: amino acids 21-40 (type II)

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FIGURE 151

GCTCCAGGGCCACGGCGGAGTCATGGTTCTCAGGACTGAGCGCTTGTTTAGGTCCGGTACTT GCCTGCGCGATCGCTGGGGGCTGCCGCGCGAAGCCGCCCGAGCCGCAGGGGGGCGCTC<u>TGA</u> GGCCGTCGGGGTGGGCACGGCCCTGGCCTAAGCTGTGCCGCCCTGGTGTGGCACTTCT CCTGCCTTCGGGCCTTGCAGCCGCCTTGCGGTGCCGCCAACCCCCGCACTCTGGTCCACGC ACGAGGCCGGGGCAAGCCGCGTGCCCCAGGCTTGGAGGAGGGGGCCTCGAGGGGGGCCGACATC CAGAGCCGAACTGAAGGGGTGAAGCCAGGGGGGCATTTATGTCGTTTGCGTAGTGGCCGCTA CTGCATCAAGGCCTACCCACTGTCTCC<u>ATG</u>CTGGGCTCTCCCTGCCTTCTGTGGCTCCTGGG GTCGAAGGTTATAAAAGCTTCCAGCCAAACGGCATTGAAGTTGAAGATACAACCTGACAGCA AAGGGGCCTGGGGGATCTCGGGCACAGACAGCCCCACCTGGGGCGCTCAGCCTGGCCCCCG CTGCTGCTTTGGGACGGCAGCGAGGCTGCGCAGAAGGGGCCCCCGCTGAACGCTACGGTCCG CCGAAGAGGGCCGCGCAGTGGTCCACTGGTGTGCCCCCTTCTCCCCGGTCCTCCACTACTGG CAGATGAGACTGAGACGGCGTGGCCGCCTTTGCCGGCTGTCCCCTGCGACTACGACCACTGC CGTGACCTTCTTGGTTCCCAGAGCTCAGCCCTTGGCCCCTCAAGACTTTGAAGAAGAGGAGG CAGCCTGAGATCTTGGGGGATCCCTCAGCCTAACACCCACAGACGTCAGCTGGTGGATTCCCU AGGACTCTCCAGCCCGGCCAGCCGCCCGACCCGCGCGCATGGGAGAAGTGCGCATTGCGG

PCT/US99/20111

FIGURE 152

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA68874
><subunit 1 of 1, 238 aa, 1 stop
><MM: 25262, pI: 6.44, NX(S/T): 1</pre>

MLGSPCLLWLLAVTFLVPRAQPLAPQDFEEEEADETETAWPPLPAVPCDYDHCRHLQVPCXE
LQRVGPAACLCPGLSSPAQPPDPPRMGEVRIAAEEGRAVVHWCAPFSPVLHYWLLLWDGSEA
AQKGPPLNATVRRAELKGLKPGGIYVVCVVAANEAGAGRVPQAGGEGLEGADIPAFGPCSRL
AVPPNPRTIVHAAVGVGTALALLSCAALVWHFCLRDRWGCPRRAAARAAGAL

Important features of the protein: Signal peptide:

amino acids 1-20

Transmembrane domain: amino acids 194-220

N-glycosylation site. amino acids 132-135

WO 00/12708 PCT/US99/20111

FIGURE 153

GAAATGGGAAAAGTGCATTTTACTGTATTTTGTGTATTTTGTTTATTTCTCAGAATATGGAA GCAATAGT CTCCAAGTCAATATAAATTCTACAGAAAATAGTGTTCTTTTTTCTCCAGAAAAAT GAAAATTTGCACATAACTTAGTTGATTCAGAAAGGACTTGTATGCTGTTTTTCTCCCAAATG CCAGTGTGATACATAGGAATCATTATTCAGAATGTAGTCTGGTCTTTAGGAAGTATTAATAA CTACCAACTAGTATATAAAGTACTAATTTAAATGCTAACATAGGAAGTTAGAAAATACTAATA CTGTGTATGACTTTTACTGAACACAGTTATGTTTTGAGGCAGCATGGTTTGATTAGCATTTCCTTCGATTCATGCAAACGAGTCACATATGGTGGGACTCGAGCCATAGTAAAGGTTGACATATAGCTT gcttgtgagaatcattaaaacatgtgacaatttagagaitctttgttttatttcactgatta AAGACTCTTTTTGACACTAAACACTTTTTAAAAAAGCTTATCTTTGCCTTCTCCAAACAAGAA CCTGGGCTTATATTACACATATAACTGTTATTTAAATACTTAACCACTAATTTTGAAAATTA gagtta<u>taa</u>aaagaaatgtcacagaagaaaaccacaaacttgttttattggacttgtgaatt AGGTGCTGAGGTTTCTGGGAATCTCCATTGGGGTGACACAAATCCTGGGCATGATTCTCACC agaaaattaaaatgtgtcaataaatattttctagagagtaa CACCTGGACAATAATTGATGCCCTTAMAATGCTGAAGACAGATGTCATACCCACTGTGTAGC CCTAAGCATATACTATTCTATGCTTTAAAATGAGGATGGAAAAGTTTCATGTCATAAGTCAC ТТТGAGTACATACTATGTGTTTTCAGAAATATGTAGAAATAAAAAATGTTGCCATAAAATAACA TGTCAAGAATCTTTGAACACACATCCATGGCAAACAGCTTTAATACACACTTTGAGATGGAG CTTGAAGAATGACAACTCTCAGCACCTGTCATGTCCCTCAGTAGAACTGTTGAAACCAAGCC CCTTTATCAACAGGGTTGTGGGAAGAAAATGTATTCCTTTTTGAGAGGAACCAAACAACTGC TCCTGCTGTGTTAGAGAATTCCCAGGATGTTCCAAACAGGCCCACCAGGAAGATCTCAGTGA gctgtggagtagtatatttcactgactggttggaaatgacagagatggactggccccagat CTACGCCCTCAATCTGCTCTTTTGGTTAATGTCCATCAGTGTGTTGGCAGTTTCTGCTTGGA AGAGAAAGAAGCGTCTCCAGCTGAAGCCAATGCAGCCCTCCGGGTCTCCGCGAAGAAGTTCC gaacttatggttccagtacaatggtcagatatggtcactttgaaaggccaggatgacaaatta TTGGAAGTTTGCTTGTCATTTTCTGTGTAGAACTGGCTTGTGGCGTTTGGACATATGAACAG TGTGGGGATGTTAGGATATTGTGGAACGGTGAAAAGAAATCTGTTGCTTCTTGCATGGTACT AITTIGACTTACTTTCCTGTGGTTCATCCGGTCATGATTGCTGTTTGCTGTTTCCTTATCAT IGAGGGACTACCTAAATAATGTTCTCACTTTAACTGCAGAAACGAGGGTAGAGGAAGCAGTC ITCTCCCTTACGGGGCTCACA<u>ATG</u>GCCAGAGAAGATTCCGTGAAGTGTCTGCGCTGCCTGCT CCCAGCGCCGACGATCGCTGCCGTTTTGCCCCTTGGGAGTAGGATGTGGTGAAAAGGATGGGGGC

EIGURE 154

><subunit 1 of 1, 305 aa, 1 stop ></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA68880

><MW: 35383, pI: 5.99, NX(S/T): 0

YYDRREPGTDQMMSLKNDNSQHLSCPSVELLKPSLSRIFEHTSMANSFNTHFEMEEL WSDMVTLKARMTNYGLPRYRWLTHAWNFFQREFKCCGVVYFTDWLEMTEMDWPPDSCCVREF VHPVMIAVCCFLIIVGMLGYCGTVKRNLLLLLAWYFGSLLVIFCVELACGVWTYEQELMVPVQ MAREDSVKCLRCLLYALNLLFWLMSISVLAVSAWMRDYLNNVLTLTAETRVEEAVILTYFFV PGCSKQAHQEDLSDLYQEGCGKKMYSFLRGTKQLQVLRFLGISIGVTQILAMILTITLLWAL

Signal peptide:

amino acids 1-33

Transmembrane domains:

amino acids 12-35, 57-86, 94-114, 226-248

FIGURE 155

CCCCGAAGGGCCTGCAGTGGCAGTCCGCCTCTCCAAGGACCGATCCACACTGCAGGTGCTGG ACTCGGCCACAGGGAACTGGTTCTCTGCCTGTTTCGACAACTTCACAGAAGCTCTGCAGGA ACAGCCTGTAGGCAGATGGGCTACAGCAGAGCTGTGGAGAATTGGCCCAGACCAGGATCTGGA CTAGAGCAAGAAACCAGTTGTAATATAAAATGCACTGCCCTACTGTTGGTATGACTACCGTT CTGGAGAGGAGGAAAGGGTCTGCGCCAGCCCTGTCCGTCTTCACCCATCCCCAAGCCTA GGAACTTTCCCACACTACTGAATGGAAGCAGGCTGTCTTGTAAAAGCCCCAGATCACTGTGGG CCATCTGTCTGCCCTTCTTTGATGAGGAGCTCACTCCAGCCACCCCACTCTGGATCATTGGA CAAACAGCACGTCTGTGGAGGGAGCATCCTGGACCCCCACTGGGTCCTCACGGCAGCCCACT TCTCAGGCTCCCTGGTCTCCCTGCACTGTCTTGCCTGTGGGAAGAGCCTGAAGACCCCCCGT CTGTGTGACGGAGAGCTGGACTGTCCCTTGGGGGAGGACGAGGAGCACTGTGTCAAGAGCTT CTGGCAAAAAAAAAAA acctactgttgtcattgttattacagctatggccactattattaaagagctgtgtaacatct AGCATCCCAGGGAGAGACACAGCCCACTGAACAAGGTCTCAGGGGTATTGCTAAGCCAAGAA TCGCAGCCCAGAGGCGCCCAGAGGAAGTCAGCAGCCCTAGCTCGGCCACACTTGGTGCTCCC AGCTTCCCATCCCTGGCTGTGGCCAAGATCATCATCATTGAATTCAACCCCATGTACCCCAA GTGGTGGGTGGGGAGGAGGCCTCTGTGGATTCTTGGCCTTBGCAGGTCAGCATCCAGTACGA TGTTGTTGAAATCACAGAAAACAGCCAGGAGCTTCGCATGCGGAACTCAAGTGGGCCCTGTC CTCGATGTCAAACCCCTGCGCAAACCCCGTATCCCCATGGAGACCTTCAGAAAGGTGGGGAT GAGAGAGGCAGCAGCTTGCTCAGCGGACAAGGATGCTGGGGCGTGAGGGACCAAGGCCTGCCC CTCTGCCCACAGCCTCAGCATTTCTTGGAGCAGCAAAGGGCCTCAATTCCTGTAAGAGACCC TGATTCTGGATAAATACTACTTCCTCTGCGGGCAGCCTCTCCACTTCATCCCGAGGAAGCAG CCCCATCATCATAGCACTACTGAGCCTGGCGAGTATCATCATTGTGGTTGTCCTCATCAAGG acceegaggatcacagagccagc<u>atg</u>ttacaggatcctgacagtgatcaacctctgaacagc CCTGTGTGGGGAGGCCCTCCTGCTGCCTTGGGGTGACAATCTCAGCTCCAGGCTACAGGGAG

PCT/US99/20111

FIGURE 156

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA68885

><subunit 1 of 1, 432 aa, 1 stop

><MW: 47644, pI: 5.18, NX(S/T): 2

MLQDPDSDQPLNSLDVKPLRKPRIPMETFRKVGIPIIIALLSLASIIIVVVLIKVILDKYYF
LCGOPLHFIPRKQLCDGELDCPLGEDEEHCVKSFPBGPAVAVRLSKDRSTLQVLDSATGNWF
SACFDNFTEALAETACRQMGYSRAVEIGPDQDLDVVEITENSQELRHRNSSGPCLSGSLVSL
HCLACGKSLKTPRVVGGEEASVDSWPWQVSIQYDKQHVCGGSILDPHWVLTAAHCFRKHTDV
FNWKVRAGSDKLGSFPSLAVAXIIIIENPMYPKDNDIALMKLQFPLIFSGTVRPICLPFFD
EELTPATPLMIIGWGFTKQNGGKMSDILLQASVQVIDSTRCNADDAYQGEVTEKMMCAGIPB
GGVDTCQGDSGGPLMYQSDQWHVVGIVSWGYGCGGPSTPGVVTKVSAYLNWIYNVWKAEL

Transmembrane domain:

amino acids 32-53 (typeII)

WO 00/12708 PCT/US99/20111

FIGURE 157

PCT/US99/20111

EIGURE 158

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA71166
><subunit 1 of 1, 761 aa, 1 stop
><MW: 83574, pl: 6.76, NX(S/T): 4</pre>

MALPALGLDPWSILIGLFLFQILIQLILPTTTAGGGGGGPMPRVRYYAGDERRALBFFHQKGLQ
DFDTILLSGDGNTLYVGAREAILALD IQDFGVPKLKMMI PWPASDRKKSECAFKKKSNETQC
FNFIRVLVSYNVTHLYTCGTFAFSPACTFI ELQDSYLLPI SEDKVMEGKGGSPFDPAHKHTA
VLVDGMLYSGTMNNFLGSEP ILMRTLGSQPVLKTDNFLRWLHHDASFVAAI PSTQVVVFFFE
ETASEFDFFERLHTSRVARVCKNDVGGEKLLQKKWTTFLKAQLLCTQFGQLPFNVIRHAVLL
PADSPTAPHI YAVFTSQWQVGGTRSSAVCAFSLLDI ERVFKGKYKELNKETSRWTTYRGPET
NPRPGSCSVGPSSDKALTFMKDHFLMDEQVVGTPLLVKSGVEYTRLAVETAQGLDGHGHLUM
YLGTTTGSLHKAVVSGDSSAHLVEE IQLFPDPEPVRNLQLAPTQGAVFVGFSGVWRVPRAN
CSVYESCVDCVLARDPHCAWDPESRTCCLLSAPNLNSWKQDMERGNPEWACASGPMSRSLRP
QSRPQI I XEVLAVPNS I LELPCPHLSALAS YYWSHGPAAVPEASSTVYNGSLLLI VQDGVGG
LYQCWATENGFS YPV I SYWUDSQDQTLALDPELAGI PREHVKVPLTRVSGGAALAAQQSYMP
HFVTVTVLFALVLSGALI I LVASPLRALRARGKVQGCETLRPGEKAPLSREQHIQSPKECRT
SASDVDADNNCLCTEVA

Signal peptide:

amino acids 1-30

Transmembrane domains:

amino acids 136-156, 222-247, 474-490, 685-704

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FIGURE 159

GCGATGTCACCATTTCTAGGGAGCTTCCCACTAGTTCTGGCAGCCCCATTCTCTAGTCCTTC GTTGGAGGCTTGATGGAAAAACCTATTAAACCAGTACCACAAGACTTGGAGAACTTCATTGC GGTTCATTAACTCTGACTTTGCCTTTGATTTTGCTCGACCTCTGCTTCCCAACACTGTTTAT CAGTATTCCCTTGCTGACTGATCACATGGACTTCTGGGGGCCGAGTGAAGAATTTTCTG GCGTTATCTCTCCCCAACCTCACTAA CGGACACAGGCTCACAGGTCTCCACATTGGGTCCCTGTCTCTGGTGCCCACAGTGAGCTCCT TACTATCTATCATGGAATAACATCCAAGAAAGACACCTTGCATATTCTTTCAGTTTCTGTTT CTIGTCCTCCTTIGTTTGCCATCAGCAAGGGCTATGCTGTGATTCTGTCTCTGAGTGACTTG TAGTTATCTCCTGTTTTCTTGAAGAACAGGAAAAATGGCCAAAAATCATCCTTTCCACTTGC GGGGCCAGAAAGGTGAAGGAGACATAAAGGCCCAGGTGCAGCCTTGGCGGGGTCTGTTTGGTGG TCACTCTGGGGACTCTATGGCTTTGTGGGAAGCTGCTGGGCATGGCTGTCTGGTGGCTGCGT TGTCTTTCAGCAGCCCTGGCATGAGCAGTACCTGTTCGACGTTTTTGTGTTTCTGCTGGGGC GGAGACCAGCCTGAAAACATGGTCCGAGTAGAAGCCCAAAAAAGTTTGGTGTTTCTATTCAGTT GGCAGAATAGCATAATGGAGGCCATCCAGCATGGTGTGCCCCATGGTGGGGGATCCCTCTCTTT CTGGCTTCCTCAGAGTGACCTCCTGGCTCACCCAAGCATCCGTCTGTTTGTCACCCACGGCG ATCCGGAAATCTTCAAGGAGATGAACAATGCCTTTGCTCACCTACCCAAGGGGTGATATGG CAAGTTTGGGGACTCTGGTTTTGTCCTTGTGACCTTGGGCTCCATGGTGAACACCTGTCAGA GGAACATTTCACAGAAGGCTCTAGGCCAGTTTTGTCTCATCTTCTACTGAAAGCAGAGTTGI ATGTTCTTTAGTTTCTGCAGGAGGCAACAGCACATGCAGTCTACATTTGACAACACCATCAA CATTCTTTCCACTTCATTCGGCTCTTTGGAATTTGGGCTACCAATCCCCTTGTCTTATGTTC GTCCTTTTATGCCAGATTTTAAAAAGGAAGAAAAATCATATCAAGTTATCAGTTGGCTTGCA TCACACCCTGACTCTTCCAGCCTCCATGTCCAGACCTAGTCAGCCTCTCTCACTCCTGCCCC AAAGAAGCTCAAGGCAGAGACATTGGCTCTTAAGATGAAA.CAAATCATGGAAGACAAGAGAT aagtgtcagtgttctcattggcccaaagatgtccacctggctgcaaatgtgaaaatttgtgga GTTGAAACTTTTGACTACTGTCCTTTCCTGATTGCTGAGAAGCCTTGGGAAGCCATTTGTGGC CCGGGTTTCTCAGATTCTTCAAGATCACGGTCATAATCTCACCATGCTTAACCACAAAAAGAG TGAGCATIGGCTGGGCAGCGAGTGCTTCTTCTAGTGGGCTTCCTTCTCCCTGGGGGTCCTGCTC ICTTGGCTGAGCAGGCATGGAGACTGTAGGTTTCCAGATTTCCTGAAAAATAAAAGTTTACA IGTTCTCCCACATATTCTCTTCAATGCTCAGGAAGCCTGCCCTGTGCTTGAGAGTTCAGGGC attettaaatagaaaggatatcatggattccttaaagaatgagaacttcgacatggtgata TCAGAGGCTGCCAAAATCCTGACAATATCTACAGTAGGTGGAAGCCATTATCTACTGATGGA AGGGTCCCTTAGCCGGGGGGGGGGGGGCGCAGCCCAGGCTGAGATCCGCGGGCTTCCGTAGAAG

FIGURE 160

LNRKDIMDSLKNENFDMVIVETFDYCPFLIAEKLGKPFVAILSTSFGSLEFGLPIPLSYVPV SAAVAASVILRSHPLSPTQRLVGWIDHVLQTGGATHLKFYVFQQPWHEQYLFDV7VFLLGLT NSIMEAIQHGVPMVGIPLFGDQPENMVRVEAKKFGVSIQLKKLKAETLALKMKQ ĮMEDKRYK EIFKEMNNAFAHLPQGVIWKCQCSHWPKDVHLAANVKIVDWLPQSDLLAHPSIRLFVTHGGQ INSDFAFDFARPLLPNTVYVGGLMEKPIKPVPQDLENFIAKFGDSGFVLVTLGSMVNTCQNP $ilde{ t r}$ $ilde{ t r}$ FMPDFKKEEKSYQVISWLAPEDHQREFKKSFDFFLEETLGGRGKFENLLNVLEYLALQCSHF MAGQRVLLLVGF1L1PGVLLSEAAK 1 LT I STVGGSHYLLMDRVSQ I LQDHGHNVTMLNHKRGP ><MW: 59581, pI: 8.68, NX(S/T): 1 ><subinit i of 1, 523 aa, 1 stop ></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA71169

amino acids 1-19 Signal peptide: LGTLWLCGKLLGMAVWWLRGARKVKET

amino acids 483-504 Transmembrane domain:

WO 00/12708 PCT/US99/20111

FIGURE 161

CCCTGGGGACCGAGTGTCTCTGCGCCTGCGTCGGGGGAATCTACTGGGTGGTTGGAAATACT GGCCCAGCCTGGATGAATCTATCAATAAAACAACTAGAGAATGGTGGTCAGTGAGACACTAT TCACTGAGTTATCTTCACTGTACCTGTTCCAGCATATCCCCCACTATCTCTCTTTTCTCCTGAT ACCATGGAAAACATCGATAACCATGCATCCTCTTGCTTGGCCACCTCCTGAAACTGCTCCAC GGCTGTCCTTCTATGCTGGATCCCAGATGGACTCTGGCCCTTACCTCCCCACCTGAGATTAG CTCTGGCTCCTTCGTAGCCCCTGTCCGGGGGTGTCTACAGCTTCCGGTTCCATGTGGTGAAGG ACCAGTGGGGCCATCTACTTCGACCAGGTCCTGGTGAACGAGGGCGGTGGCTTTGACCGGGC GAGTGGCATTTGCTGCGGTCCGAAGCCACCACCATGAGCCAGCAGGGGAAAACCGGCAATGGC GCCTGGCCGAGCTGCAGGGGGGCCCGGGGGAGCAGCCCTGGGAGAGGGCACCCCTGGGC AGACCGGGGCACTTGTGGGTTGCAGAGCCCCTCAGCCATGTTGGGAGCCAAGCCACACTGGC TGTTGCAGAGGAAAATAAATATCAAACTGTATACTAAAATTAAAAA agaattactaaggagaagatgcctctggagtttggatcgggtgttacaggtacaagtaggta GGTGAGTGTGTTTGCTCTGGCTGAGAGCAGAGCTGAGAGCAGGTATACAGAGCTGGAAGTGG TCAGCCAGCACCGTCAGAAGCTGAGCCAGCACCGTATGGGCTAGGGTGGGAGGCTCAGCCAC ATGGACAAGCCTCAGCGTACCCTGCAGGCTTCTTCCTGTGAGGAAAGCCAGCATCACGGATC TGTACAACCGCCAAACTGTCCAGGTGAGCCTGATGCTGAACACGTGGCCTGTCATCTCAGCC GGGTGGGCCCAGGAGGGGTCAGAGCCCCGTCCTGCTGGAGGGGGAGTGCCTGGTGGTCTGTGA AGACTATCAGGGTGCCGGCGGTGAGAATCCAGGGAGAGGAGCGGAAACAGAAQAGGGGCAGA gggaggcaggacagagctgggacacaggtatggagagggggttcagcgagcctagagaggggc ACTGCTGTCACTGCATGCTCTGCCAAGGAGGAGGGAACTGCAGTGACAGCAGGAGTAAGAG ITTGCCAATGATCCTGACGTGACCCGGGAGGCAGCCACCAGCTCTGTGCTACTGCCCTTGGA

PCT/US99/20111

FIGURE 162

><subunit 1 of 1, 205 aa, 1 stop ></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA71180

><MW: 21521, pI: 7.07, NX(S/T): 1

SFRFHVVKVYNRQTVQVSLMLNTWPVISAFANDPDVTREAATSSVLLPLDPGDRVSLRLRRG MLGAXPHWLPGPLHSPGLPLVLVLLALGAGWAQEGSEPVLLEGECLVVCEPGRAAAGGPGGA NLLGGWKYSSFSGFLIFPL ALGEAPFGRVAFAAVRSHHHEPAGETGNGTSGAIYFDQVLVNEGGGFDRASGSFVAPVRGVY

amino acids 1-32 Signal peptide:

> WO 00/12708 PCT/US99/20111

FIGURE 163

GCCAATTCCCTGGAGGAACCAGCTGCAAATCACTTTTTTGCTCTGTAAATTTGGAAGTGTCA $\mathtt{CAAGACCAAGTTCGGCCTCCCGGAGACTGAGGTTCCTGGAGGTGAAC\underline{TGA}GCCAGCCTTCGGG}$ CAAGACATCGACCTGTACCACACCATGTACATGGAGGCCCTGGTGAAGCTCTTCGACAAGCA ATGCATCTTCCATGGTCGAGGCCTCTTCTCCTCCGACACCTGGGGGGCTGGTGCCCTACTCCA GAGGAGGGCTCCTGGGGCCGATGGGTCCAGAAGAAGTTCCAGAAATACATTGGTTTCGCCCC GAGCTGACCTGGTTCCCATCTACTCCTTTGGAGAGAATGAAGTGTACAAGCAGGTGATCTTC GGGAGTGGCAATGCTATCATCATCGTGGTCGGGGGTGCGGCTGAGTCTCTGAGCTCCATGCC CATACGGCCTTACCTGGCTACACTGGCAGGCAACTTCCGAATGCCTGTGTTGAGGGAGTACC GGCCTGGGTGCCTTCTGCAACTTCAGCACAGAGGCCACAGAAGTGAGCAAGAAGTTCCCCAGG GTGGGTCCGAAACTGGGGCTGTGTGGCGCTACTTTCGAGACTACTTTCCCCATCCAGCTGGTGA CTCTACTTCACTTGGCTGGTGTTTGACTGGAACACACCCAAGAAAGGTGGCAGGAGGTCACA GAGTGGCCTGCAGTGCCATCCTCATGTACATATTCTGCACTGATTGCTGGCTCATCGCTGTG GAAGCCAGCGCTCTCACGGAGGACCTGCCCTGTCGCGCGAGGGGGTCTGGGAGATGGGGCACT AAAAAAAAAAAAAAAAAA AGCCCATCACCACTGTTGTGGGAGAGCCCCATCACCATCCCCAAGCTGGAGCACCCAACCCAG TGGCAAGAATGCAGTCACCCTGCGGAACCGCAAGGGCTTTGTGAAACTGGCCCTGCGTCATG TGATGTCTGGAGGTATCTGCCCTGTCAGCCGGGACACCATAGACTATTTGCTTTCAAAGAAT AGACACAACCTGCTGACCACCAGGAACTATATCTTTGGATACCACCCCCATGGTATCATG GGATCCAGCATCCTCCGGCCCTCCAGGACCTCTTCTCTGTCACCTGGCTCAATAGGTCCAA **Q**AAGACCCTCATAGCCGCCTACTCCGGGGTCCTGCGCGGCGAGCGTCAGGCCGAGGCTGACC GGGCCAGGGGGGGGGAAGCGGCTTCCCGGGGGGCCGTGACTGGGGGGGTTCAGCCAT GCTGTTTCTCTCGCGCCACCACTGGCCGCCGGCGGCAGCTCCAGGTGTCCTAGCCGCCCAGC CTCGACGCCGTCCCGGGACCCCTGTGCTCTCCGCGAAGCCCT3GCCCCGGGGGCCGGGGCAT

FIGURE 164

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA71184
><subunit 1 of 1, 388 aa, 1 stop
><MM: 43831, pI: 9.64, NX(S/T): 3</pre>

MKTLIAAYSGVLRGERQAEADRSQRSHGGPALSREGSGRWGTGSSILSALQDLFSVTWLNRS
KVEKQLQVISVLQWVLSFLVLGVACSAILMYIFCTDCWLIAVLYFTWLVFDWNTFKKGGRRS
QWVRNWAVWRYFRDYFPIQLVKTHNLLTTRNYIFGYHPHGIMGLGAFCNFSTEATEVSKKFP
GIRPYLATLAGNFRMPVLREYLMSGGICFVSRDTIDYLLSKNGSGNAIIIVVGGAAESLSSM
PGKNAVTLRNRKGFVKLALRHGADLVPIYSFGENEVYKQVIFEEGSWGRWVQKKFQKYIGFA
PCIFHGRGLFSSDTWGLVFYSKPITTVVGEPITIPKLEHPTQQDIDLYHTMYMEALVKLFDK
HKTKFGLPETEVLEVN

Important features of the protein: Transmembrane domain: amino acids 76-97

N-glycosylation sites. amino acids 60-63, 173-176, 228-231

N-myristoylation sites. amino acids 10-15, 41-46, 84-89, 120-125, 169-174, 229-234, 240-245, 318-323, 378-383

, 66/270

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FIGURE 165

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FIGURE 166

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA71213
><subunit i of 1, 368 ma, 1 stop</pre>

><MW: 42550, pI: 9.11, NX(S/T): 1

MGLLAFLKTQFVLHLLVGFVFVVSGLVINFVQLCTLALMPVSKQLYRRLNCRLAYSLMSQLV
MLLEMWSCTECTLFTDQATVER.FGKEHAVIILNHNFEIDFLCGWTMCER.FGVLGSSKVLAKK
ELLYVPLIGWTWYELEIVFCKRKWEEDRDTVVEGLRRLSDYFEYMWELLYCEGTR.FTETKHR
VSMEVAAAKGLPVLKYHLLPRTKGFTTAVKCLRGTVAAVYDVTLNFRGNKNPSLLGILYGKK
YEADMCVRRFPLEDIPLDEKEAAQWLHKLYQSKDALQEIYNQKGMFPGEQFKPARRPWTLLN
FLSWATILLSELFSFVLGVFASGSPLLILTFLGFVGAASFGVRRLIGESLEPGRWRLQ

Important features of the protein: Signal peptide:

Signal peptide:

amino acids 1-25

amino acids 307-323, 335-352

Transmembrane domains:

Tyrosine kinase phosphorylation sites. amino acids 160-168, 161-169

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FIGURE 167

GATGGTGTAGGGCCCAGCATTGTAAATTCACACGTTGACTGTGCTTGTGAATTATCTGGGGA CTTGTTTAATGCTCTCATAAGACCACTTGTTTCCCTTTTTGCAGCACTTGCCACTCAGTTGTA ACATGTGGTGTTCTCTTGTCGTTCCTGTAATGTGGTATGCCATGGGGTCTTTGCACAAGCCT GATAGCTGGGGTCTGAGACCTGCTTCCTCAGTAAAATTCCTGGGATCTGCCTATACCTTCTT agagtgagactctatgtccaaaaaaaaaaaaa AACCTGGGAGGCGGAGGTTGCAGTGAGCCGAGATCAGGCCACTGTATTCCAACCAGGGTGAC GGCATGGTGGCACATGCCTGTAGTCCCAGCTACTTGGGAGGCTGAAGCAAGAGAATCGCTTG TCAAGACTAGCCTGGCCAACATGGTGGAACCCCATCTGTACTAAAAATACACAAATTAGCTG TGCTGGTCCTATGAACTATACTAAATAGTAAGAATCTATGGAGCCAGGCTGGGCATGGTGGC TGCAGGTCCTGATTCAGTAGGCCCAGGTTGGGCATCTCTAACAAACTCCCACGTGATGCTGA CATGTTTTAGAGACTAAATGGAGGAGGAGATGAGGAAAAGATTGAAATCTCTCAGTTCACCA TCTTTATGTGCGTTTGTGTTGTATGGGTTGTGTCTGTTCCCCAGAATGCCCAGCTCTGAGC ATCCTGCAGATTTCAATTCTAACATCATTTTCTCCAGGGATCCTGGCCTGACAGAATCTCAT TICCTCTTTGGCTGGACACTGTTCCCTGCCCCCCCATACTCTTCCTACTTAATATGTAGTC AGTATTTAGAGCTACAAGAGCCCTCATGGTCTGGCCCCTGCCCCCTGGCCAGCTTCATTGT TTCTCTAACCTGGCATACCCTGCTTAAAGCCTCTCAGGGCTTCTCTCTGTTCTTAGGATCAA GCCACCAGGCATATTCATCTTTGTGTGTGTTTTTTCTTTTGCTTTAGCACTGGGGCACTTCTT GATATTCTTTATTTTTAAGAATCTGAAGTACT<u>ATG</u>CATCACTCCCTCCAATGTCCTGGGGCA

FIGURE 168

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA71234

><subunit 1 of 1, 143 aa, 1 stop

><MW: 15624, pI: 9.58, NX(S/T): 0

MHSLQCPGAATRHIHLCVCFSFALALGHFLLISLVGKGLSLSCGVGGRQAGLRLIRPWVRR

EGKINFYTNGDSWGLRPASSVKFLGSAYTFFSLTWHTLLKASQGFSLFLGSKYLELQEPSWS GPCPPGQLHCTCGVLLSFL

Important features of the protein:

Signal peptide:

amino acids 1-28

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FIGURE 169

CAATTTAAATCATGTTCTAGTAATTGGAGCTGTCCCCAAGACCAAAGGAGCTAGAGCTTGGT TCAAATGATCTCCAAGGGCCCTTATACCCCAGGAGACTTTGATTTGAATTTGAAACCCCAAA TCCAAACCTAAGAACCAGGTGCATTAAGAATCAGTTATTGCCGGGTGTGGTGGCCCTGAATG CCAACATTTTGGGAGGCCGAGGCGGGTAGATCACCTGAGGTCAGGAGTTCAAGACCAGCCTG GCTCAGTGTTGGCCCAGGAGGTCAGCAAGGCCTGAGAGCTGATCAGAAGGGCCTGCTGTGGGGAACAGGAAATGCCCCAGGTAAGCACAGGCTGCAAAATCCCCCAGGCAAAGGACTGTGTGGGCT GCTGCGGCTTTCAAGGTGGGCCTTGCCCTGGCCGTAGAAGGGAT<u>TGA</u>CAAGCCCGAAGATTT CATAGGCGATGGCTCCCACTGCCCAGGCATCAGCCTTGCTGTAGTCAATCACTGCCCTGGG ACCAACTGTCTCACGTCTGGAGGCACTGACTCGGGCAGTGCAGGTAGCTGAGCCTCTTGGTA ACCUTCCCCCCGAAGCCGGGGACAGCCTCACCTTGCTGGCCTCTCGCTGGAGCAGTGCCCTC CACTGTGGCTCTGGCCCAAACCTGACCTTCACTCTGGAACGAGAACAGAGGTTTCTACCCAC $\mathtt{AGGAGTTGAACTGCTAGGATTCTGACT}_{\mathtt{ATG}}\mathtt{CTGTGGTGGCTAGTGCTCCTACTCCTACCTAC}$ GGCTGGACTGGAACTCCTGGTCCCAAGTGATCCACCCGCCTCAGCCTCCCAAGGTGCTGTGA
TTATAGGTGTAAGCCACCGTGTCTGGCCTCTGAACAACTTTTTCAGCAACTAAAAAAGCCAC **AAAATAAAAAAGAATTATGGTTATTTGTAA** GÄAGGAGGCTGAGACAGGAGAATCACTTCAGCCTGAGCAACACAGCGAGACTCTGTCTCAGA GTGTGCCTGTATCCCAGCTACTCGGGAGGCTGAGACAGGAGAATTACTTGAACCTGGGAGGT GCCAACATGGTGAAACCCCTGTCTCTACTAAAAATACAAAAAAACTAGCCAGGCATGGTGGT TGAGAGGCCCTCCTATGTCCCTACTAAAGCCACCAGCAAGACATAGCTGACAGGGGCTAATG CCAGGGGCAGCCGTCTGGGAAGGAGCAAGCAAAGTGACCATTTCTCCTCCCCCTCCTTCCCTC AAGGGCAACTGCAGGCCGATGCTCTCATCAGCCAGGCAGCCAAAAATCTGCGATCACCAG CGGGACTCACCTCTGGGGCCATCAGACAGCCGTTTCCGCCCCGATCCACGTACCAGCTGCTG ATCGAGTCTCCTGCATTCAGTGGACATGTGGGGGGAAGGGCTGCCGATGGCGCATGACACACT GGGAAGGAACTTGTGCCAAATTATGGGTCAGAAAAGATGGAGGTGTTGGGTTATCACAAGGC TATGTGACAGGACTTGCATTCTCCTGGAACATGAGGGAACGCCGGAGGAAAGCAAAGTGGCA ATTAAAATCTGTTTTTTGTTCTCTTGTAACTAGCCTTTACCTTCCTAACACACAGGATCTG1

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FIGURE 170

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA71277

><subunit 1 of 1, 109 aa, 1 stop

><MW: 11822, pI: 8.63, NX(S/T): 0

MLWWLVLLLLPTLKSVFCSLVTSLYLPNTEDLSLWLWPKPDLHSGTRTEVSTHTVPSKPGTA

SPCWPLAGAVPSPTVSRLEALTRAVQVAEPLGSCGFQGGPCPGRRRD

Signal peptide:

amino acids 1-15

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IGURE 171

CTAGGGCTGGCCCCTAGTGAGTGGGCTCGAGGGAGGGTTGCCTGGGAACCCCCAGGAATTGAC GACGTCAGGGTCTACATCAGCCTCCTGCCCCCTGGGCGATGGACTCACCTTGGCCTTCAAGAT GCTGCTGCGACCCGGAGGCATCCTCGCCGTCCTCAGAGTCCTGTGGCGCGGGAAGGTGCTGC GCCCCGGAGCTGGGACGCCCCTGTGGAGGCAGGCCGAGGCGGAGCACAAGATCGACCTCC CTGGCCCTGGCCCTGGCGCCCGCGGACGGGCGCGTGGTGACCTGCGAGGTGGACGCGCA TGGCGCGGCTCATCCAGGCCAAGAAGGCGCTGGACCTGGGCACCTTCACGGGCTACTCCGCC CCTGGAGCAGCCGCAGGGGGATTCTATGATGACCTGCGAGCAGGCCCAAGCTCTTGGCCAACC CAGTATCTTCTGAGCCGCTCCATGCGGGAGCACCCGGCGCTGCGAAGCCTGAGGCTGCTGAC GCCCCCATGGCGAGGCCGGCGAGAGCAGTGCCTGCTTCCCCCCGAGGACAGCCGCCTGTGG GGCCCTGGGCTCAGCCGCACTGGGCGCCGCCTTCGCCACTGGCCTCTTCCTGGGGAGGCGGT CCGCCGCTCCTGCCGCGCALGNCCCAAGCCGGTGCCCCCCTCTCCCGTGCCCGCCGCGCT GCGGGCCCGCGAGTCCGAGACCTGTCCCAGGAGCTCCAGCTCACGTGACCTGTCACTGCCTC

FIGURE 172

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></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA71282
><subunit 1 of 1, 262 aa, 1 stop
><www.28809, pI: 8.80, NX(S/T): 1
MTOPVPRLSVPAALALGSAALGAAFATGLFLGRRCPPWRGRREQCLLPPEDSRLWQYLLSRS
WREHPALRSLRLLTLEQPQGDSMMTCEQAQLLANLARLIQAKKALDLGTFTGYSALALALALAL
PADGRVVTCEVDAQPPELGRPLWRQAEAEHKIDLRLKPALETLDELLAAGEAGTFDVAVVDA
DKENCSAYYERCLQLLRPGGILAVLRVLWRGKVLQPPKGDVAAECVRNLNERIRRDVRVYIS</pre>
```

Important features of the protein:

Signal peptide:

amino acids 1-25

Transmembrane domains:

amino acids 8-30, 109-130

N-glycosylation site.

amino acids 190-193

Tyrosine kinase phosphorylation site.

amino acids 238-246

N-myristoylation sites.

amino acids 22-27, 28-33, 110-115, 205-210, 255-260

Amidation sites.

amino acids 31-34, 39-42

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FIGURE 173

GACTCAGACAAGAGTAGCGACAACAGTGGCCTGAAGAGGGAAGACGCCTGCGCTAAAGATGTC CCCAGCTCAGGCTGCCCCTCTCCTTCCCCGGCTCGCAGGAGCAGAGCAGAGAACTGTGGG ${ t GGGGGACTCGGAGGCCCTGGACGAGGGAGAGCCTGA}_{ t GCCGCGGGCAGCCAGGCCCAGCCCCCGC}$ GTACGGGAGGGTCCCGACCTGGACAGGCCTGGGAGCGACCGGCAGGAGCGCGAGAGGGCACG AGCCCCAGTGAATGGCGAGGCCACATCACAGAAGGGGGAGAGCGCAGAGGACAAGGAGCACG GAGCTGGCCCGGGAGGAGGCCCCCCAGGAGAAGGCGGAGGACAAGCCCAGCACCGATCTCTC GAAGGCAGCAGAAGTCTATACCCGGCTCAAGTCGCGGGTCCTCGGCCCAAAGATCGAGGCGG ACAGACGTGGTGGCCACCTTGAAGAAGATTCGCCGTTACAAAGCGAACAAGGACGTAATGGA GCCTGAATGCCCTAGAGGAGCTGGGAACCCTGCAGGTGACCTCTCAGATCCTCCAGAAGAAC GCAGAAGCTGCACAGTGAGATCAAGTTTGCCCCTAAAGGTCGACAGCCCGGACGTGAAGAGGT GAGGGCTTCTCGATGGACAGGAAGGTAGAGAAGAAGAAGAAGACCCTCCGTGGAGGAGAAGCT GCGGAGGCGCGAGCGGGCCGACCGGGGGAGGCTGAGCGGGGCAGCGGCGGCAGCAGCGGG GCGGAAACCGAAGCCTGAACGGCCTCCGTCCAGCTCCAGCAGTGACAGTGACAGCGACGACGAGG TCTGTGAAGAAGCCTCCGAGGGGCAGGAAGCCAGCGGAGAAGCCTCTCCCGAAGCCGCGAGG GGCGCCGTCAGCCTCCGACTCCGACTCCAAGGCCGATTCGGACGGGGCCAAGCCTGAGCCGG AAGAGGAGAACTCGGAAAGCTCATCTGAGTCGGAGAAGACCAGCGACCAGGACTTCACACCT GGTCTCGAAACGAGCCCGAAAGGCCTCCAGCGACCTGGATCAGGCCAGCGTGTCCCCATCCG GGGTCATGGCCGTCACAGCGGTAACCGCCACAGCTGCCAGCGACAGGATGGAGAGCGACTCA CGAGGCCCCCGAGGCCAACCCCGCCGACGGCAGTGACGCTGACGAGGACGATGAGGACCGGG GAGATCCAGAACAACCCCCACGCCAGCTACAGCGCCCCTCCGCCAGTGAGCTCCTCCGACAG acaaatgtaaagacaagtacgggaagcccaacaagaggaaaggcttcaatgaagggctgtg CATCTTTTTCTTTGGCACACACGAAACAGCCTTCCTGGGACCCAAGGACCTGTTCCCCCTACG GC<u>ATQ</u>CCACACGCCTTCAAGCCCCGGGGACTTGGTGTTCGCTAAGATGAAGGGCTACCCTCAC CCGCCGCCGCAGCCGCTACCGCCGCTGCAGCCGCTTTCCGCGGCCTGGGCCTCTCGCCGTCA aggagggt coggacteggaggagggecaaggtstegeteetetaagaeetgeaegaeage igcagaaagtgaacaaggctgggatggagaaggagaaggccgaggagaagctggccggggag TGGACCGCATCAGTGAGTGGAAGCGGCGGGACGAGGCGCGAGGCGCGAGCTGGAGGCCCGG

FIGURE 174

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA71286
><subunit 1 of 1, 671 aa, 1 stop</pre>

WHAFK PGDLUFAKMKGYPHWPAR IDDIADGAVKPPPNKYPIFFFGTHETAPLGPKDLFPYD
KCKDKYGKPNKRKGFNEGLMEIQNNFHAASYSAPPPVSSSDSEAPPANPADGSDADEDDEDRG
VMAVTAVTATAASDRMESDSDSDKSSDNSGLKRKTPALKMSVSKRARKASSDLDQASVSPGE
EENGESSSESEKTSDQDFTPEKKAAVRAPRRGFLGGRKKKKAPSASDSDSKADSDGAKPEPV
AMARSASSSSSSSDSDVSVKKPPRGRKPAEKPLPKPRGRKPKPERPPSSSSSSDSDSDEV
DRISEWKRHDEARRRELEARRREGEEELRRLREGEKEEKERRRERADRGEAERGSGGSSGD
ELREDDEFVKKAGRKGRGPPSSSDSEPBAELEREAKKSAKKPOSSSTEPARKPGQKEKRV
RPEEKQQAKPVKYERTRKRSEGFSMDRKVEKKKEPSVEEKLQKLHSEIKFALKVDSPDVKRC

Signal peptide: amino acids 1-13

egrdseegprcgssedlhdsvægpdldrpgsdrqererargdsealdees

LNALEELGTLQVTSQILQKNTDVVATLKKIRRYKANKDVMEKAAEVYTRLKSRVLGFKIEAV QKVNKAGMEKEKAEEKLAGEELAGEEAPQEKAEDKPSTDLSAPVNGBATSQKGBSAEDKEHE

WO 00/12708 PCT/US59/Z0111

FIGURE 175

FIGURE 176

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA71883
><subunit 1 of 1; 777 aa, 1 stop</pre>

><MW: 89651, pI: 7.97, NX(S/T): 3

MNANKDERLKARSODFHLFPALMMISMTMIFLPVTGTIKQNIPRIKLTYKDILLSNSCIPFI
GSSEGLDFQTILLLDEERGRLLIGAKDHIFILSLVDLNKNFKKIYMPAAKERVELCKLAGKDA
NTECANFIRVLQPYNKTHIYVCGTGAPHPICGYIDLGVYKEDIIFKLDTHNLESGRLKCPFD
PQQPFASVMTDEYLYSGTASDFIGKDTAFTRSIGPTHDHHYIRTDISEHYMLMGAKFIGTFF
IPDTYNPDDDKIYFFFRESSQEGSTSDKTILSRVGRVCKNDVGGQRSLINKWTTFIKARLIC
SIPGSDGADTYFDELQDIYLLPTRDERNPVVYGVFTTTSSIFKGSAVCVYSMADIRAVFNGP
YAHKESADHRWVQYDGRIPYPRPGTCPSKTYDPLIKSTRDFPDDVISFIKRHSVMYKSVYPV
AGGPTFKRINVDYRLTQIVVDHVIAEDGQYDVMFLGTDIGTVLKVVSI8KEKWNMEEVVLEE
LQIFKHSSIILNMELSLKQQQLYIGSRDGLVQLSLHRCDTYGKACADCCLARDPYCAMDGNA
CSRYAPTSKRRARRQDVKYGDPITQCWDIEDSIGHTADEKVIFGIEFNSTFLECIPKSQQA
TIKWYIQRSGDEHREELKPDERIIKTEYGLLIRSLQKKDSGMYYCKAQEHTFIHTIVKLTLN
VIENEQMENTQRAEHEEGQVKDLLAESRLRYKDYIQILSSPNFSLDQYCEQMWH3EKRRQRN
KGGPKWKHMQEMKKKRNRRHHRDLDELPRAVAT

Important features of the protein:

Signal peptide:

amino acids 1-36

N-glycosylation sites.

amino acids 139-142, 607-610, 724-727

amino acids 571-576

Tyrosine kinase phosphorylation site

Gram-positive cocci surface proteins 'anchoring' hexapeptide.

amino acids 32-37

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FIGURE 177

AMARCAGTGACAATCCCTTGCGGGGCAGAGCCCACAGGATTCCTTGGCACAGGCCCTGTACAGLTACACTGACAGACGACAGA СССТВАССТВСТВЛЯССАЛСАТВЛЯСТВВЛЯСВСВЕЛЯВАССВЕЛЯВАСВТЭТСТВВЛЯСА,ТВССЛССВСВВВЛЯСАЛСЬ СВССТВЛЯСТВВЛЯСЬ СТСАБСЛЯТТВЛЯСЬСАБЛЕСТВВЛЯСЬ СТСАБСЛЯТТВЛЯСЬ В СВСТВВЛЕСТВВЛЯСЬ В СВСТВВЛЯСТВВЛЯСТВВЛЯСТВВЛЯСТВВЛЯСЬ В СВСТВВЛЯСТВВ TCTCAATGTGTGTCACCCGGAACCTGGGAGGGGAGGGAACACTGGGGTTTAGGACCACAACTCAGAGGGCTGCTTG GCCCTCCCCTTTGACCAGGGACATCCTGAGTTTGGTGGCTACTTCCCTTCTGGCCTAAGGTAGGGAAGGCCTTCTC ngggaagattaaatgacntaatgtatgtg<u>ang</u>caactagcaaagtaccagtcccatagtaagtaagcagcagcagcagcagagct Dattecaacccacccctgttctctggccttcccaaccagtactgcaacgactagagcagagaggcggcaggaggct agccattgagggtgtcatggagctacagaggggagagggaaaggtattttaaggtaacagtgtggcacaatagttai GGGTGAGGTGGGGGGGGCACAGGTGTCATGTGCACCTTCTTGTCTCAGCAAGAAGAGCTGAGAAGAGGGGGATCTTGG KANGITTIGITIACGITCTTICAGCATGCTCCTTAAAACCCCAGAAGCCCCAATTTCCCCCAAGCCCCATTY KITCTIGICCTTATCTAATAAACTCAATATTAAG INGATTSTISGEGEACATTSTISTAGCCTGACTTCTGCTGGAGCTCCCAGTTCCAGGAGGAAAGAACCAAGGCCAACTT XTCCTGTCCCCACCAGAGCCCCAGCTCCTGTCTGTGGGGGAGCCATCACGGTGTTCGTGCAGTCCATAGCGCT

17/2/2

FIGURE 178

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA73401</pre>

><subunit 1 of 1, 370 aa, 1 stop

><MW: 40685, pI: 4.53, NX(S/T): 0

DFEECEETGELFEEPAPQALATRALPCPAHVVFRYQAGREDELTITEGEWLEVIEEGDADEW QVSQVKGAARLALLQGAGLDVERWLKPAMTQAQDEVEQERRLSEARLSQRDLSPTAEDAELS EGALIRLLPRAQDGVDDGFWRGEFGGRVGVFPSLLVEELLGPPGPPELSDPEQMLPSPSPPS VKARNQHGEVGFVPERYLNFPDLSLPESSQDSDNPCGAEPTAFLAQALYSYTGQSAEELSFP MQLAXYQSHSKSCPTVFPPTPVLCLPNQVLQRLEQRRQQASEREAPSIEQRLQEVRESIRRA FSPPAPTSVLDGPPAPVLPGDKALDFPGFLDMMAPRLRPMRPPPPPPAKAPDPGHPDPLT

> WO 00/12708 PCT/US99/20111

FIGURE 179A

CTITIGACIONES CONTRETARIOS CONT OCCCTAGACGGCCTCAGTCCCTCCCAGCTGCAGTACCAGTGCC<u>ATG</u>TCCCAGACAGGCTCGCATCCCGGAGGGG CACAGGGAGACCCCACAGACACATATGCACGAGAGAGACAGAGGAGGAAAGAGACACAGAGACAAAGACACACAGCGGA

FIGURE 179B

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WO 00/12708 PCT/US99/20111

FIGURE 180

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA73492</pre>

><subunit 1 of 1, 837 ma, 1 stop
><MM: 90167, pI: 8.39, NX(S/T): 1
MSQTGSHPGRGLAGRWIMGAQPCLLLPIVPLSWLVWLLLLLLLASLLPSARLASPLPREEEIV</pre> MPSPTDVVLPGAVSLRYSGATAASETLSGHGPLAQPLTLQVLVAGNFQDTRLRYSFFVPRPT LTCQARALGYYYVLEPRVVDGTPCSPDSSSVCVQGRCIHAGCDR1IGSKKKFDKCMVCGGDG CEGRRTRFRSCNTEDCPTGSALTFREEQCAAYNHRTDLFKSFPGPMDWVPRYTGVAPQDQCK PAQACMGGRCLHMDQLQDFNIPQAGGWGPWGPWGDCSRTCGGGVQFSSRDCTRPVPRNGGKY ${ t DTAILFTRQDLCGVSTCDTLGMADVGTVCDPARSCAIVEDDGLQSAPTAAHELGHVFNMLHD}$ AAKAFKHPSIRNPVSLVVTRLVILGSGEEGPQVGPSAAQTLRSFCAWQRGLNTPEDSGPDHF ASGQGPMCNVKAPLGSPSPRPRRAKRFASLSRFVETLVVADDKMAAFHGAGLKRYLLTVMAA GTYLTGTINGDPESVASLHWDGGALLGVLQYRGAELHLQPLEGGTPNSAGGPGAHILRRKSP PPEKINGSVLPGSGAPARLLCRLQAFGETLLLELEQDSGVQVEGGLTVQYLGQAPELLGGAEP PSTPRPTPQDWLHRRAQILEILRRRPWAGRK SGCSKQSGSFRKFRYGYNNVVTIPAGATHILVRQQGNPGHRSIYLALKLPDGSYALNGEYTL PVTFPGKDYDADRQCQLTFGPDSRHCPQLPPPCAALWCSGHLNGHAMCQTKHSPWADGTPCG NSKPCI SLNGPLSTSRHVMAPVMAHVDPEEPWSPCSARFI TDFLDNGYGHCLLDKPEAPLHL

Important features of the protein:

Signal peptide:

amino acids 1-48

N-glycosylation site.

amino acids 68-71

Glycosaminoglycan attachment site

amino acids 188-191, 772-775

amino acids 182-185 cAMP- and cGMP-dependent protein kinase phosphorylation site.

Tyrosine kinase phosphorylation site.

amino acids 730-736

N-myristoylation sites.

Amidation sites.

172, 168-173, 174-179, 323-328, 352-357, 539-544, 555-560, 577-582, 679-684, 682-687, 763-768

amino acids 5-10, 19-24, 121-126, 125-130, 130-135, 147-152, 167-

amino acids 560-563, 834-837

Leucine zipper pattern.

amino acids 17-38, 24-45

amino acids 358-367 Neutral zinc metallopeptidases, zinc-binding region eignature.

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FIGURE 181

CTCCAGAATTACTTGTAGGTAATTCCTCTCTTCATGTTCTAATAAACTTCTACATTATCACC AATAAATGCATGCTATTCAATGAATTTCTGCCTATGAGGCATCTGGCCCCTGGTAGCCAGCT CGAGGCAACCGCTATTGCCGCCGCGTCTGTGAACCTTTACTAGGCTACTACCCATATCCATA AAAATGGAATAGAATTTGATCCCATGCTGGATGAGAGAGGTTATTGTTGTATTTACTGCCGT CCACTCTAATATCAGTTTCTGAGTTACAAGACTTTGAGGAGGAGGAGGAAGATCTTCACTTT TAAAAACGGATACACTGGCATCTACTTCGTGGGTCTTCAAAAATGTTTTATCAAAACTCAGA ACCAGAACTGAAATATTCAGAAGCGGAAATGGCACTGATGAAACATTGGAAGTGCACGACTT TGGAGCACACTTTCTACAGCAATGGAGAGAAGAAGAAGATTTACATGGAAATTGATCCTGTG AATTGTCCTGTTTTGGGGGAGCAAGCACTTCTGGCCGGAGGTACCCAAAAAAGCCCTATGACA AAGAAAATATGTAAATCACTTAAGATTTGTGGACTGGTGTTTGGTATCCTGGCCCTAACTCT CAAAGAATCCTCCAGAGAATTGTGAAGACTGTCACATTCTAAATGCAGAAGCTTTTAAATCC GCATGCTGGGGAGGGTC<u>TAA</u>TAGGAGGTTTGAGCTCAAATGCTTAAACTGCTGGCAACATAT AGAGAAGACCCGTCACGCCAGACAAGCAAGTGAGGAAGAACTTCCAATAAATGACTATACTG TTTTCTTAAAAATTCCAAAATTCTGGAGATTTGTGATAACGTGACCATGTATTGGATCAATC ACAACTTTCTTTGAACAGTCAGTGATTTGGGTCCCAGCAGAAAAGCCTATTGAAAACCGAGA TTAAAGTGATTCCTGAATTTTCTGAACCAGAAGAGGAAATAGATGAGAATGAAGAAATTACC

/84/270

WO 00/12708 PCT/US99/20111

FIGURE 182

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA73727

><subunit 1 of 1, 317 aa, 1 stop

><MW: 37130, pI: 5.18, NX(S/T): 3

TENGIEFDPMLDERGYCCIYCRRGNRYCRRVCEPLLGYYPYPYCYQGGRVICRVIMPCNWWV NPTLISVSELQDFEEEGEDLHFPANEKKG1EQNEQWVVPQVKVEKTRHARQASEEELPINDY QIKVIPEFSBPEEEIDENEEITTTFFEQSVIWVPAEKPIENRDFLKNSKILEICDNVTMYWI DMEHTFYSNGEKKKIYME IDPVTRTE IFRSGNGTDETLEVHDFKNGYTG IYFVGLQKCFIKT MAKNPPENCEDCHILNAEAFKSKKICKSLKICGLVFGILALTLIVLFWGSKHFWPEVPKKAY

Important features of the protein:

Signal peptide:

amino acids 1-40

Transmembrane domain:

amino acids 25-47 (type II)

N-glycosylation sites.

amino acids 94-97, 180-183

Glycosaminoglycan attachment sites.

amino acids 92-95, 70-73, 85-88, 133-136, 148-151, 192-195, 239-

N-myristoylation sites.

amino acids 33-38, 95-100, 116-121, 215-220, 272-277

amino acids 315-317

Microbodies C-terminal targeting signal

Cytochrome c family heme-binding site signature.

amino acids 9-14

185/270

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FIGURE 183

ATGTGAATGCGAGGAAATGTCTTTAGAGCACAGGGGACAGAGGGGGGAAATAAGAGGAGGAGAA AATGGAGGCAGGGGTTCCAGCACAAAGTTTACTTCTGGGCAATTTTTTGTATCCAAGGAAATA CAGGGCCACCACGACCACTGCAAACACCGCACCTGCCTACCAGCCACCAGCTGCCTACAAAG GGCACCCTGCTTTGCCTGTCCTGCCAGGACGAGGCACCCTACAGGCCCTACCAGGCCCCGCC GCGCCTGCGCCGTCATCGGGATGAAGTGCACGCGCTGCGCCAAGGGCACACCCCGCCAAGACC GCTCAGCTTCCTGGGCATGGTGGGCACGTTGATCACCACCCATCCTGCCGCACTGGCGGAGGA ACAATCGGGCCCCCCCAGTGACCTCGGCCACGCACAGCGGGTACAGGCTGAACGACTACGTG AGTTTGAGATTGGCCAGGCCCTGTACCTGGGCTTCATCTCCTCGTCCCTCTCGCTCATTGGT CTCCTGGACCACCAACGACGTGGTGCAGAACTTCTACAACCCGGTGCTGCCCAGCGGCATGA TGTGTGTGGCACAGCACAGGCATCTACCAGTGCCAGATCTACCGATCCCTGCTGGCGCTGCC CGGCTGGCCTAGGCAGGCAGCCGCACCATTGGCCAGCACGGCCGTGCAGCTTCTGGGCTTCCT GCGGAACTGGCTCCGGCTGGCACCTGAGGAGCGGCGTGACCCCGAGGGCCCAGGGAGCTGCC ttatgtgggtgatttgataacaagtttaatataaaagtgacttgggagtttggtcagtggggt

WO 00/12708 PCT/US99/20111

FIGURE 184

MASTAVOLLGELLSELGMVGTLITTILPHWRRTAHVGTNILTAVSYLKGLMMECVMHSTGIY
QCQIYRSLLALEQDLQAARALMVISCLLSGIACAVIGMKCTRCAKGTPAKTTEAILGGTL
FILAGLLCMVAVSWTTNDVVQNFYNPLLESGMKFEIGQALYLGFISSSLSLIGGTLLCLSCQ
DEAPYRPYQAPPRATTTIANTAPAYQPPAAYKDNRAPSVTSATHSGYRLNDYV

Important features of the protein:

Signal peptide:

amino acids 1-21

Transmembrane domains:

amino acids 82-103, 115-141, 160-182

FIGURE 185

GCATACACCTGTAGTCCCAGCATTCCGGGAGGCTGAGGTGGGAGGATCACTTGAGCCCAGGG GGCAACATGGAGAAGCCCTGTCTCTACAAAATACAGAGAGAAAAAATCAGCCAGTCATGGTG GAAGCAATAAGAGAAAGATATTTGTAATCTCTCCAGCCCATGATCTCGGTTTTCTTACACTG ATTTTGATGATTTAGACAGACTCCCCCCTCTTCCTCCTAGTCAATAAACCCATTGATGATCTA TCCTGTCTAAAAAAATAAAAATAAATAATGGAACACAGCAAGTCCTAGGAAGTAGGTTAAA CTAGCACTTTGGGAGGCTGAGGAGGAAGGATCACTTGAGCCCAGAAGTTCGAGACTAGCCTG ATATGGTA CTTTGTAAAGTCATGCTTAAGTACAAATTCCATGAAAAGCTCACACCTGTAATC aatagcct cacccctacatgtggatagaaggaaatgaaaaaataattgctttgacattgtct ttaagtoctaaatatagttaaaataaataatgttttagtaaaatgatacactatctctgtga CTGTTGACATCTTCTTATTACAGCAACACCATTCTAGGAGTTTCCTGAGCTCTCCACTGGAG TGATCTTAAAAGTTACCAAACCAAAGTCATTTTCAGTTTGAGGCAACCAAACCTTTCTACTG CTGCTGTTTGAATTTTGTCTCCCCACCCCCAACTTGGCTAGTAATAAACACTTACTGAAGAA AACAAGGAGATCCCATCTAGATTTCTTCTTGCTTTTGACTCACAGCTGGAAGTTAGAAAAGC TGTG<u>TAA</u>TGCTCTAAGACCTCTCAGCACGGGGGGAAGAAACTCCCGGAGAGCTCACCCAAAA ATATACGATGGAGGTGCCCGCACAGAGGACGAGGTACAATCTTATCCTTCCAAGCACGACTA CCTACAAGCCTGGAGGCTTCAAGGCCAGCACTGGCTTTGGGTCCAACACCAAAAAAACAAGAAG CCTGGCACCAGAAGAAACCAACTACAAAGCCGTTTCTTATCATGCCTCAGGCCACAGTGTTG GGCTGGGTCGCTGGAGGCCTCACACTAATTGGGGGTGTGATGATGTGCATCGCCTGCCGGGG **GCATGGGTGGGATGGTGCAGACTGTTCAGACCAGGTACACATTTGGTGCGGCTCTGTTCGTG** GTCTGTGTTTGCCAACATGCTGGTGACTAACTTCTGGATGTCCACAGCTAACATGTACACCG AACATGACACTGACCTCCGGGATCATGTTCATTGTCTCAGGTCTTTGTGCAATTGCTGGAGI TGGTATCCATCTTTGCCCTGAAATGCATCCGCATTGGCAGCATGGAGGACTCTGCCAAAGCC CATGCTGCAGGCAGTGCGAGCCCTGATGATCGTAGGCATCGTCCTGGGTGCCATTGGCCTCC GTGAGGCAGAGTTCAGGCTTCACCGAATGCAGGCCCTATTTCACCATCCTGGGACTTCCAGC AGGACCTGTACGACAACCCCGTCACCTCCGTGTTCCAGTACGAAGGGCTCTGGAGGAGCTGC GAGCTCCCCTCAGGAGCGCGTTAGCTTCACACCTTCGGCAGCAGGAGGGCGGCAGCTTCTCG

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FIGURE 186

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA73734
><subunit 1 of 1, 261 aa, 1 stop</pre>

><MW: 27856, pI: 8.50, NX(S/T): 1

MSTTTCQVVAFLLSILGLAGCIAATGMDMMSTQDLYDNPVTSVFQYEGLWRSCVRQSSGFTE
CRPYFTILGLPAMLQAVRALMIVGIVLGAIGLLVSIFALKCIRIGSMEDSAKANMTLTSGIM
FIVSGLCAIAGVSVFANMLVTNFWMSTANMYTGMGGMVQTVQTRYTFGAALFVGMVAGGLTL
IGGVMMCIACRGLAPEETNYKAVSYHASGHSVAYKPGGFKASTGFGSNTKNKKIYDGGARTE
DEVQSYPSKHDYV

Signal peptide:

amino acids 1-23

Transmembrane domains:

amino acids 81-100, 121-141, 173-194

FIGURE 187

ATCTGTAAATACTGTATTTTTCTGTTTATTCCAAATTTGATGAAACTGACAATCCAATTTGA AAGTTTGTGTCGACGTCTGTCTAGCTTAAATGAATGTGTTCTATTTGCTTTTATACATTTATA TCATTTTTGTTCTGTGAAAAATAAATTTCCTTCTTGTACCATTTCTGTTTAGTTTTACTAAA TTITITAGCCTAGGAGTTAGAAATCCTAACTTCTTTAICCTCTTCTCCCAGAGGCTTTTTTTT
TTCTTGTGTAITAAATTAACATTTTTAAAACGCAGATATTTTGTCAAGGGGCTTTGCATTCA GTTGCCCAAAAACGTGAGCTTGGAGAAGCTCTCTACTTAGGATGGACCACGGCACTGGTGCT TCATCCCTGTGAGCTGGGTTGCCAATGCCATCATCAGAGATTTCTATAACTCAATAGTGAAT GGTGAAGGCTCACATTCTGCTGACGGCTGGAATCATCTTCATCATCACGGGCATGGTGGTGC GAGTCCAGCTGGCTAAAACTCATCCCAGAGGATA<u>ATG</u>GCAACCCATGCCTTAGAAATCGCTG GGCTGTTTCTTGGTGGTGGTGGAATGGTGGGCACAGTGGCTGTCACTGTCATTGCCTCAGTGG ACAAAAAAGTTGTCCTTTGAGAACTTCACCTGCTCCTATGTGGGTACCTGAGTCAAAATTG GAAATCATATATGTATGGATATATTTTAATAAGTATTTGAGTACAGACTTTGAGGTTTCATC AACTGCTTTTCCAGGGCTATACTCAGAAGAAAGATAAAAGTGTGATCTAAGAAAAGTGATG agattaaaatgaaggctttaatcagcattgtaaaggaaattgaatggctttctgatatgctg GCTATTTCAGCAGAATGAGATATTAAACCCCAATGCTTTGATTGTTCTAGAAAGTATAGTAAT CTGTTCTTAACTGCCTAATCTTAATTACAGGAACTGTGCATCAGCTATTTATGATTCTATAA CATGCAAATGACAAAATCTATATTACTTTCTCAAAATGGACCCCAAAGAAACTTTGATTTA GATACTCGATACCTTCCCATCGCACAACCCAAAAAAGTTATCACACCGGAAAGAAGTCACCG GATTGTTGGAGGAGCTCTGTTCTGCTGCGTTTTTTTGTTGCAACGAAAAGAGCAGTAGCTACA TTGGCTTTCATGATGGCCATCCTTGGCATGAAATGCACCAGGTGCACGGGGGACAATGAGAA CTCTTTCTCCGGACCTACAGGCAGCCAGAGGACTGATGTGTGCTGCTTCCGTGATGTCCTTC GATGAATTGCGTGAGGCAGGCTAACATCAGGATGCAGTGCAAAATCTATGATTCCCTGCTGG AGAGTGTCGGCCTTCATTGAAAACAACATCGTGGT1'I'TIGAAAACTTCTGGGAAGGACTGTG aagaaggttactattaaitgtttaaaaacagcttagggattaatgtcctccatttataatga agcgtctactccagaagtcagtatgtg<u>tag</u>ttgtgtatgttttttttaactttactataaagc GGAAAAACIGTTCTCTTCTGTGGCACAGAGAACCCCTGCTTCAAAGCAGAAGTAGCAGTTCCG

WO 00/12708 PCT/US99/20111

FIGURE 188

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA73735
><subunit 1 of 1, 225 aa, _ stop</pre>

><MW: 24845, pI: 9.07, NX(S/T): 0

MATHALEIAGLFLGGVGMVGTVAVTVMPQNRVSAFIENNIVVFENFWEGLMMNCVRQANIRM
QCKIYDSLLALSPDLQAARGLMCAASVMSFLAFMMAILGMKCTRCTGDNEKVKAHILLTAGI
IFIITGMVVLIPVSMVANAIIRDFYNSIVNVAQKRELGEALYLGMTTALVLIVGGALFCCVF
CCNEKSSSYRYSIPSHRTTQKSYHTGKKSPSVVSRSQYV

Signal peptide:

amino acids 1-17

Transmembrane domains:

amino acids 82-101, 118-145, 164-188

PCT/US99/20111

FIGURE 189

CCCCCCATCCTACTCAGGTCTCTGGAGCTCCTCTCTTCACCCCTGGAAAAACAAATCATCTG GCCATCTCTCGGGGGCCCTCTGAGTACCCTACCAAGAATTACGTCTGACGTGGAGGGGAATG AATGGCCTGGTCTCCTGTGCCCTGCCCATGTGGAAGGTGACCGCTTTCATCGGCAACAGCAT CTTCTGCCCTGCCCCCCCCCCCCCCCCTTTACACTCACATTTTTATCAAATAAAGCATG TCCACCCCCAGGGCCAGGTCCCAGCTATGTAGACCCCCGCCCCCACGTCCAACACTGCACC TTAACAAAGGACTGCCCACCTCCGGAACTTCTGACCTCTGTTTCCTCCGTCCTGATAAGACG ATGATGGAGCCAAAGAGGGGATGCTTTGAGATTCTTGGATCTTGACATGCCCATCTTAGAAGC GAAAACTGAGCCAAGGTGTTGACTCAGACTCTCACTTAGGCTCTGCTGTTTCTCACCCTTGG CGTACCTTTTGTTTCTGCCTCCTGCTATTTTTCTTTTGACTGAGGATATTTAAAATTCATTT GGGGCTCCGCTGGCGCTAGAGCCATCCAGAAGTGGCAGTGCCCAACAGCTTTGGGATGGGTT GCCCTTCGGGGGGGTCCCAGGGCCCAGCCATTACATGGCCCGCTACTCAACATCTGCCCCT ATCCGGGACTTCTATAACCCCCTGGTGGCTGAGGCCCAAAAGCGGGAGCTGGGGGCCTCCCT TTGTCTTTGTCATCTCAGGGGTCCTGACGCTAATCCCCGTGTGCTGGACGGCGCATGCCATC CAAGTGTACCACCTGTGTGGAGGAGAAGGATTCCAAGGCCCGCCTGGTGCTCACCTCTGGGA GCCCTCTGTGTCATCGCCCTCCTTGTGGCCCTGTTCGGCTTGCTGGTCTACCTTGCTGGGGC AGATGCAGTGCAAGGTGTACGACTCACTGCTGGCGCTGCCACAGGACCTGCAGGCTGCACGT CGTGGTGGCCCAGGTGGTGTGGAGGGCCTGTGGATGTCCTGCGTGGTGCAGAGCACCGGCC TGTCCCCAAGAGTTCCTGCTGCTGGGGGCTGGGCTTCCCTAGATGTCACTGGACAGCTG TCGCC<u>ATG</u>GCCTCTGCCGGAATGCAGATCCTGGGAGTCGTCCTGACACTGCTGGGCTGGGTG

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FIGURE 190

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA73736</pre>

><8ubunit 1 of 1, 220 aa, 1 stop ><MW: 23292, pI: 8.43, NX(S/T): 0

MASAGMQILGVVLTILGWVNGLVSCALPMWKVTAFIGNSIVVAQVVWEGLMMSCVVQSTGQM QCKVYDSLLALPQDLQAARALCVIALLVALFGLLVYLAGAKCTTCVEEKDSKARLVLTSGIV FVISGVLTILIPVCWTAHAIIRDFYNPLVAEAQKRELGASLYLGWAASGLLLLGGGLLCCTCP SGGSQGPSHYMARYSTSAPAISRGPSEYPTKNYV

Transmembrane domains:

amino acids 8-30 (type II), 82-102, :21-140, 166-186

FIGURE 191

GCCAAGGAGAACATCATCAAAGACTTCTCTAGACTCAAAAGGCTTCCACGTTCTACATCTTG TGTACAATGATGGACTACTTATTACTTTTTGACCATCATGTATTATCTGATAAGAATCTAAA GAACTTGCTTTATGTCTAGATTTACATTGATACGAAAGTTTCAATTTGTTACTGGTGGTAGG **GTTGAAATTGATATCTATAACAATAAAACATATACCTATTCTA** GACCCAATCGCTGCTCCAATTTTCATATTCTAAATTCAAGTATACCCATAATCATTAGCAAG GGGTATCTTCGTTCTGATTCCGGTGAGCTGGACAGCCAATATAATCATCAGAGATTTTCTACA GGCTCTAACGAGAGGGCCAAAGCATACCTTCTGGGAACTTCAGGAGTCCTCTTCATCCTGAC TTGCTCTCTCTTGATCGCCCTGCTTATTGGCATCTGTGGCATGAAGCAGGTCCAGTGCACA TTGCAAATTGCTGGGCTGGTTCTTGGGTTCCTTGGCATGGTGGGGACTCTTGCCACAACCCT aatgaaaatgacttacttggacattctgacttcaggtgtattaaatgcattgactattgttg ATGGACTATGGTCAATGTTTTTTATAMAGTCCTGCTAGAAACTGTAAGTATGTGAGGCAGGA ATACGACAATGCTTAGTAAGACCTCCACCAGTTATGTC<u>TAA</u>TGCCTCCTTTTGGCTCCAAGT AGCGCTGCTGTCCTCCTTCATTGGAGGGGGTCTGCTTTGTGGATTTTGCTGCTGCAACAGAAA ACCCAGCCATCCACATAGGTCAGAAACGAGAGCTGGGAGCAGCACTTTTCCTTGGCTGGGCA TCTGCCTCAGTGGTGGAGTATCAGCTTTTGTTGGCAGCAACATTATTGTCTTTGAGAGGCTC AGCATCTTCTACCACTCCGAATTGAACCAGTCTTCAAAGTAAAGGCAATGGCATTTTATCCC

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FIGURE 192

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA73737
><subunit 1 of 1, 173 aa, 1 stop</pre>

><MW: 18938, pI: 9.99, NX(S/T): 1

MNCIROARVRLQCKFYSSLLALÞPALETARALMCVAVALSLIALLIGICGMKOVQCTGSNER AKAYLLGTSGVLFILTGIFVLIFVSMTANIIIRÐFYNFAIHIGQKRELGAALFLGMASAAVL FIGGGLLCGFCCCNRKKQGYRYÞVÞGYRVÐHTDKKRNTTMLSKTSTSYV

Important features of the protein:
Transmembrane domains:
amino acids 31-51, 71-90, 112-133

N-glycosylation site.
amino acids 161-164

FIGURE 193

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FIGURE 194

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA73739

><subunit 1 of 1, 85 aa, 1 stop
><MW: 9232, pI: 7.94, NX(S/T): 0</pre>

MKITGGLLLLCTVVYFCSSSEAASLSPKKVDCSIYKKYPVVAIPCPITYLPVCGSDYITYGN ECHLCTESLKSNGRVQFLHDGSC

Signal peptide:

amino acids 1-19

FIGURE 195

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FIGURE 196

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA73742

><subunit 1 of 1, 148 aa, 1 stop ><MW: 17183, pI: 8.77, NX(S/T): 0

MAASPARPAVLALITGIALLLLLCWGPGGISGNKLXLMLQKREAPVPTKTKVAVDENKAKEFL GSLKRQKRQLWDRTRPEVQQWYQQFLYMGFDEAKFEDDITYWLNRDRNGHEYYGDYYQRHYD EDSAIGPRSPYGFRHGASVNYDDY

Signal peptide: amino acids 1-30

PCT/US99/20111

FIGURE 197

CTGGGAGTGGGCTCCTCGGGGTCGGGCATCTGCTGTCGCTGCCTCGGGCCCCGGGCAGAGCCG CCTCTTCCCGCTGCCCTGGAGCCCAGCCCTGCGCCAGAGGACTCCCCGGGACTGGCGGAGG GCCTTTGCCATGTACCGCCCGTAGTGCCTCCGCGGGCGCTTGGCAGCGTCGCCGGCCCCTCC GCTGCTGCCCCTGCTGCTGCTGCTGCTGCTGCTGGTACTGCCAGATCCAGTACCGGC CCAAATCCCCCCTGCCCGGGGTCCGAGCCCGGGCCCCTCCGGGCTGGAAATCGGCAGCCT CGTCCTTTTCTCGGTGCTTGCCTGCCTTCTGGTGCTGGCCTTGCCTGGGTCTCAACGCACA AGCTCCTTGGGCTGAGTTGGGGACGCCAGGTCGGTGGAGGCTGGTGAAGGGGAGCGGGGAG GGCCGCCCGGGGGGCCCGTCTTAGTGTTCTGCCGGAGGACCCAGCCGCCTCCAATCCCTGAC CCCCGCCCTGCGACCGCCGGGGCTCGGGGGCCACCTCCCGGGGGCTGCTGAACCTCAGCCCGCA CCTTCTTTCCCCTGACCGCCACTCTGGGCCTGGCCGGCTTCACCCTGCTCCTCAGTCTCCTG GCAGCCTTCACCTCCCTCCCAACTGCGTTCTCCACTGCCACGTGTCCACGAGAGTCGGTCCC GGAACAGCAGGTGCGACTCATCTACCAAGGGCAGCTGCTAGGCGACGACACCCCAGACCCTGG GTGGCCAGGGCCTGGCCCCACGACACCATTGGCTCCTTGAAAAAGGACCCAGTTTCCCGGCCG CCCCGGACTCCCCGCAGGAGCCCCCTCGTGCTACGGCTGAAATTCCTCAATGATTCAGAGCAG GAGACACAGAGGTCAAGCTGCACAGCCAGAGCCCAGCACGGGGTTCACAGCAACACCGCCAG GCAGCCATGGCAGCTACCGACAGCATGAGAGGGGGAGGCCCCAGGGGGCAGAGACCCCCAGCCT CCGCTGAGGGCGGGGACCCACTGCCCCAGCCGTCAGGGACCCCAACGCCATCCCAGCCCAGC GGTAGCGCGGCGGCAAGGCAGGCGCC<u>ATG</u>ACCCTGATTGAAGGGGTGGGTGATGAGGTGAC CGGCTCGAGCCCGCGGAAGTGCCCGAGGGGCCGCGATGGAGCTGGGGGAGCCGGGCGCTC

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FIGURE 198

MTLIEGVGDEVTVLFSVLACLLVLALAWVSTHTAEGGDPLPQPSGTFTFSQPSAMAATDSM
RGEAPGAETPSLRHRGQAAQPEESTGFTATPPAPDSFQEPLVLRLKFLNDSEQVARAWPHDT
IGSLKRTQFFGREQQVRLIYQGQLLGDDTQTLGSLHLFNCVLHCHVSTRVGPPNPPCPPGS
EPGFSGLEIGSLLLFLLLLLLLLLLWYCQIQYRPFFFLTATLGLAGFTLLLSLLAFAMYRP

Signal peptide: amino acids 1-31

.

Transmembrane domain: amino acids 195-217

PCT/US99/20111

FIGURE 199

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FIGURE 200

></usr/seqdb2/ssc/DNA/Dnaseqs.min/ss.DNA73746</pre>

><subunit 1 of 1, 148 aa, 1 stop ><MW: 16896, pI: 6.05, NX(S/T): 1

MTKALLIYLVSSFLALNQASLISRCDLAQVLQLEDLDGFEGYSLSDWLCLAFVESKFNISKI NENADGSFDYGLFQINSHYWCNDYKSYSENLCHVDCQDLLNPNLLAGIHCAKRIVSGARGMN NWVEWRLHCSGRPLSYWLTGCRLR

Signal peptide: amino acids 1-18

1/2/0

FIGURE 201

GTGTGCTCCTTGTGTTAGGAGAGAAAAAAGCTCTATGAAAGAATATAGGAAGTTTCTCCTTT aaaatccagctccaagtgaacgtaaagagcttatatatttcatgaagctgatccttttgtgt gataaatgctgtggatgaacga<u>tga</u>atgtcaatgtcagaaggaaaagagaattttggccatc AATAAAGATTTGTACCTGCGTCCGTGTGATGGAAAAGCCCGCCAGCAGTGGCGATTTGACCA GATTCTTCAGAACTGCACGGAGGAAGGCCTGGCCATCCACCAGCAGCACTGGGACTTCCAGG GTCCCATGGTGTTGGCTCCTTGCAGTGACAGCCGGCAGCAACAGTACCTGCAGCACACCAGC GCTCCACAACACTGGACTTGGGCTCTGTGCAGACTGCCAGGCAGAAGGGGACATCCTGGGCT GTCATTCAAAGAAACCTTCTACAAGCATAGCCCAGAGGCCTTCTCCTTGAGCAAGGCTGAGA GCTCTGTTGAAATCCTTCCCTGCTCTCGGGTAGGACACATCTACCAAAATCAGGATTCCCAT GTGCCCGGAGAGGTGGTGGCCATGGACAGACATTACTTCCAAAACACTGGAGCGTATGACTC GGTGACAGGAGCCGAGTGGTATCTCCGGTGATAGATGTGATTGACTGGAAGACTTTCCAGTA GCTGGGTGCCATCAGGGCCCGGATGCTGGGGGCCACCAGAGCCACCGGGGATGTGCTCGTCT GTGGCCTCCAGGAGGCACTCAGTGCCCGCATCCCCCTCCAGAGGGCTCTGCCCGAGGTGCGG GCCTGATGAGGACGGGGAGGTGTCTGAAGAAGAGAGTTGACCCCGTTCAGCCTGGACCCAC TGCTGGTGGCCGTGGCCTTACCCCAGGCCAGAAGGAACCAGAGCCAGGGCAGGAAGAGGTGGG GGGTGAAGAGTACAGCCCTCTGGAGGGCCTGCCACCCTTTATCTCACTGCGGGAGGATCAGC GAAGCCAGGTACCGCCTGGACTTTGGGGAATCCCAGGATTGGGTACTGGAAGCTGAGGATGA CAGACTCCAGTTCCTGCTGCTGCTGCTGATGCTGGGATGCGTCCTGATGATGGTGGCGATGT CTGTTGCATTTGGCAAGTTCTAGCAAC<u>ATG</u>CTCCTAAGGAAGCGATACAGGCACAGACCATG ACCCATGTTCTGCTGCAAGCTTGAAGGAGCCTGGAGCGGGAGAAAGCTAACTTGAACATGAC TTGGGGTGAAACTTGGGTCCTGTGGTTTTCTGATTGTAAGTGGAAGCAGGTCTTGCACACGC aattigaagteeetgigaatgggettieagaaggeaattaaagaaateeacteagagaggae CCAGCTCATCCCAGACACCTCATAGCAACCTATTTATACAAAGGGGGAAAAGAAACACCTGAG agaatgggatgatygtccacattctttctgggaaatgcatggaagctgtggtgcaagaaaac ITTCTGGCTAATGTCTACCCTGAGCTGTACCCATCTGAACCCAGGCCCAGTTTCTCTGGAAA AGCCAGACTGCATGGAACGCTTGCAGCTGCAAAGGAGACTGGGTTGTCGGACATTCCACTGG ICTTATGTCGCTGCGAGGTGGTGAAAACCTCGAACTGTCTTTCAAGGCCTGGCTCTGTGGTG CTTTGCCAGAGCATGTGAGGAAGGCCCTCCAGTCCCCCATAAGCCCCCATCAGGAGCCCCTGTG TTACCCCTCAAAGGACCTGCAGCGTGGGGTGTTGGACTGGAAGCTGGATTTCCACTGGGAAC TCATGGATGCCCACTGCGAGTGCCACCCAGGCTGGCTGGAGCCCCTCCTCAGCAGAATAGCT TCTGCTCTCAGCGAATATGTGGCCAGGCTGGAGGGGGGTGAAGTTACTCAGGAGCAACAAGAG TTTCCATGATGAGGCCTGGTCCACTCTCCTGCGGACTGTACACAGCATCCTCGACACAGTGC AGCTACCGCCTCATCAAGCAGCCAAGGAGGCAGGATAAGGAAGCCCCAAAGAGGGACTGGGG TGTTGGCAAATGTCAGGACCAGGTTAAGTGACTGGCAGAAAAACTTCCAGGTGGAACAAGCA TCTGACCTGACTGGAAGCGTCCAAAGAGGGACGGCTGTCAGCCCTGCTTGACTGAGAACCCA **PCACACCITATTTCATTGACTGCTGGCTGCTTA**

204,270

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FIGURE 202

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA73760

><subunit 1 of 1, 639 aa, 1 stop
><MW: 73063, pI: 6.84, NX(S/T): 2</pre>

MILRKRYRHRPCKLQFILLLIMLGCVLMMVAMLHPPHHTLHQTVTAQASKHSPEARYRLDFG
ESQDWVLEAEDEGEEYSPLEGLPFTISLREDQLLVAVALPQARRNQSQGRRGGSYRLIKQPR
RQDKEAPKRDWGADEDGEVSEEEELTPFSLDPRGLOEALSARIPLQRALPEVRHPICLQOHP
QDSLPTASVILCFHDEAWSTLLRTVHSILDTVPRAFLKEIILVDDLSQQGQLKSALSEYVAR
LEGVKLLRSNKRLGAIRARMLGATRATGDVLVFMDAHCECHPGWLEPLLSRIAGDRSRVVSP
VIDVIDWKTFQYYPSKDLQRGVLDWKLDFHWEPLPEHVRKALQSPISPIRSPVVPGEVVAMD
RHYFQNTGAYDSLMSLRGGENLELSFKAWLCGGSVEILPCSRVGHIYQNQDSHSPLDQEATL
RNRVRIAETWLGSFKETFYKHSPEAFSLSKAEKPDCMERLQLQRRLGCRTFHWFLANVYPEL
YPSEPRPSFSGKLHNTGLGLCADCQAEGDILGCPMVLAPCSDSRQQQYLQHTSRKEIHFGSF
QHLCFAVRQEQVILQNCTEEGLAIHQQHWDFQENGMIVHILSGKCMEAVVQENNKDLYLKPC
DGKARQQWRFDQINAVDER

Signal peptide:

amino acide 1-28

FIGURE 203

TCTGGTCCCATTCCACACCATTTGTTTCTCTGTGTCCCCCATCCTACTCCAAGGATGCCGGCA
TCACCCTGAGGGCTCCCCCCTTGGGAATGGGGTAGTGAGGCCCCAGACTTCACCCCCAGCCCA
CTGCTAAAATCTGTTTTCTGACAGATGGGTTTTTGGGAGATCGCCTGCTCCACTACATGAGAA CTTCTCCCAGTCTCTCAGGATCTGTGTCCTATTCTCTGCCCATAACTCCAACTCTGCCC
TCTTTGGTTTTTTCTCATGCCACCTTGTCTAAGACAACTCTGCCCTCTTAACCTTGATTCCC GACCTGTCCCCGGCTGGAGTCACTGTGCTGGGGGGCCTTCGGGGGACTCACCCTACCCCACCCC CATCATTGTTCTCGTGGCCACTGGCATCATCTTCAAGTTCTGCTGGGACCGCAGCCAGAAGC CTGTTCGGGGGCCGTGGGGAAGGTGTGGACCCCCAGCTCTATGTCACAATTACCATCTCCAT GTGATATATATTTTTGTATTATCTCTTCTTCTTCTTGTGGTGATCATCTTGAATTACTGTG CCCTTTGGGCCTCCCTAACTCCACCTAGGCTGCCAGGGACCGGAGTCAGCTGGTTCAAGGCC GTGCTGCTCCAGAGGTGGGTGAGGTGAGCTGGGGGGCTCCTTGGGCCCTCATCGGTCATGG TGTGCGGCGTGCTCACTCTCCCCTCATGAACACCCACCACCTCGTTTCCGCAGCCCCTGC TGGTCAGCGTTTCCTGCACACTTTACCTCTCATGTGCGTTTCCCGGCCTGATGTTGTGGTGG AGGCCATTTGCACACGCTCCTGCACCCTCTCCCCGTCCATACCGCTCCGCTCAGCTGACTCT GGTCCCTGTCCCCACCCTTGTGCACTCACATGAAAGCCTTGCACACTCACCTCCACCTTCAC CCACGGGCAATCCTATCTGCTCGCCCTCCTGCAGGTGGGGGCCTCACATATCTGTGACTTCG GCTGGGGCCACAGGGGCTCCTGGCTCCTGCCCCTTGCACACCACCCGGAACACTCCCCAGCC aagcaggaggecaaggggecggcacageeeccateecactgagggtggggcagetgtgggga TCCCTCTTCCTCTCAGGATTCCCCTGGTGAATCTGTGATGCCCCCAATGTTGGGGTGCAGCC CCTCTTTGTCTTGAACTTCCCCTTCTATTCTGGCCTACCCCTTGGTTCCTGACTGTGCCCTT CTCCCACAGCCCCTGGCCCTCCCAAGGGGGCTGGACCAGCTCCTCTCTGGGAGGCACCCTTC CCTTCCAGTTGAACCGG<u>TGA</u>GGGCAGGGGCAATGGGATGGGAGGGCAAAGAGGGAAGGCAAC TGACCATGAGGAGCCCCGAGGGGGACCCCGGCCTGGGATGCCCCACCCCAAGGGGGCTCCAG CCATGCGAGGTGATGGAGATGGGCTTATCCTTGGAGAGGCACCTGCCACCCTGCGGCCATTC ATTICTGGACTATGGTTTTGCAGCCCCTCATGGGCTCGCAACCCCCACACCCCAACTCAGACT ATCGTGTGGGGTCCCACCGTGTCTCGAGAGGATGGAGGGGACCCCAACTCTGCCAATCCCGG CACCCCAGCCACCCCATCAGGCTTTGAGGAGGGGCCGCCCTCATCCCAATACCCCTGGGCT TGCCCCTCCCACCGCCTGCTCAGGGCTCTTCATCCTCCCCTCGAACCCCACCAGCCCCAGCC CGCCAAGCATGCAGTAAAGGCTGAAAATCTGGGTCACAGCTGAGGAAGACCTCAGAC<u>ATg</u>GA GGATGTAAGTTTCAAAATTTTCAAATAAAGCCTTTGCAAGATAA CTTCCCTCCTTCTCACTGGTTTTTCCACCTTCCTCCTTCCCTTCTTCCCTGGCTCCTAGGCT TCTGTGTGTGCGATTCTCTGGACTTCAGAGCCCCTGAGCCAGTCCTCCCTTCCCAGCCT

205/270

WO 00/12708 PCT/US99/20111

FIGURE 204

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA76393

><subunit 1 of 1, 243 aa, 1 stop

><MW: 26266, pI: 8.43, NX(S/T): 1

MRPQGPAASPQRLRGLLLLLLLQLPAPSSASEIPKGKQKAQLRQREVVDLYNGMCLQGPAGV PGRDGSPGANVIPGTPGIPGRDGFKGEKGECLRESFEESWTPNYKQCSWSSLNYGIDLGKIA ECTFTKMRSNSALRVLFSGSLRLKCRNACCQRWYFTPNGAECSGPLFIEAIIYLDQGSPEMN STINIHRTSSVEGLCEGIGAGLVDVAIWVGTCSDYPKGDASTGWNSVSRIIIEELPK

Signal peptide:

amino acids 1-30

Transmembrane domain:

amino acids 195-217

FIGURE 205

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FIGURE 206

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA76398

><subunit 1 of 1, 121 aa, 1 stop

><MW: 12073, pI: 4.11, NX(S/T): 0

MASCLALRMALLLIVSGVLAPAVLTDDVPQEPVPTLMNEPAELPSGEGPVZSTSPGREPVDTG PPAPTVAPGPEDSTAQERLDQGGGSLGPGATAAIVTAALLATCVVLALVVVALRKFSAS

Important features of the protein:

Signal peptide:

amino acids 1-19

Transmembrane domain:

amino acids 91-110

Glycosaminoglycan attachment site.

amino acids 44-47

cAMP- and cGMP-dependent protein kinase phosphorylation site. amino acids 116-119

N-myristoylation site. amino acids 91-96

FIGURE 207

GGGGCCCCCAGGGAGGGAGGCAGGGGGGGGGGACATGGAGAGCTGAGGCAGCCTCGTCTCC CCTGGGACACACAGAGCCACCCGGGCTTGTGAGTGACCCAGAGAAGGGAGGCCTCGGGAGAAAAAGGGGTGCTCGGAACACCCTTCCGAACACCCTCCAGGC GCCAGGGCCCTACTGTCCCTGGGGTCCCAGGCTCTCCTTGGAGGGGGGCTCCCCGCCTTCCAC GAGGGAATGGGGGTGGGCTGTGCGCAGCATCAGCGCCTGGGCAGGTCCGCAGAGCTGCGGGA GTGGGGGGGAAACTCAGCTGGACAGCCCCTGCCTGTCACTCTGGAGCTGGGCTGCTGCTGC TGGAAGATGCTGCTGAGTGTCTCAAGCAGCACTGACAGCAGCTGGGCCTGCCCCAGGGCAAC CCGCAGCCTGGTATCGCCAGCCTTAAGGTGTCTGGAGCCCCCACACTTGGCCAACCTGACCT acgagggtgtcctggatgtggccacacataggaccacacgtcccagctgggaggaggaggcct CTCTGCAACCACACCCATGTGGTGGTTTCATGAACAGACCACGCTCCTCTGCCTTCTCCTGG AGATCAGTGGGGGCACTGCAGGTGGGGGCTCTCCCTATACCTGGGACACCTGCTGGATGTCAC CCTGACCTGGACTTCAGGGGGAGGGGGTAAAAGGGAGAGAGGAGGGGGGCTAGGGGGTCCTCT ATGGAGGGGCTGACTGCCCCACATTGCCTTTCAGACAGGACACGAGCATGAGGTAAGGCCGC ACCCCATCCCAGGTCTGTGGTCAGAGCCTGGGAGGGTTCCCTACGATGGTTAGGGGGTGCCCC GTCTCCGACCCTCAGCTGGAGGCGGGCATCTTTCCTAAAAGGGTCCCCATAGGGTCTGGTTCC GGAGGTGGAACCTCAACCCAGCTCTGCGCAGGAGGCGGCTGCAGTCCTTTTCTCCCTCAAAG CGACTGTCAGCACCGCTGTGGCATCTTCCAGTACGAGACCATCTCCTGCAACAACTGCACAG CCAGAGGCGCTGGGAGTGTTGCCACCGCCCTCCCCTGAAGTTTGCTCCATCTCACGCTGGGG ACCCAGCCTAGCACCTGAAGGATCAATGCCATCACCCCGGGGGGCCTCCCC<u>TAA</u>GTAGCCC CCGGGTATTTCCCCAACGAGCTGCGAAACATCTTCCGGGAGCAGGTGCACCTCATCCAGAAC CCAAGTGGCGACAGCAGTGTACCAGATGATGGATCAGCTGTACCAGGGGAAGATGTACTTCC GACGACACGATGAAGGAGCTGCACCTGGCCATCCCCGCCAAGATCACCCGGGAGAAGCTGGA <u>ACTTCAAGTCCTGGTGGGTGGGCGACATCCCCGTGTCAGGGGGCGCTGCTCACCGACTGGAGC</u> CGGCTGTCTGCACTGCCACAGCAACTTCTCCAAGAAGTTCTCCTTCTACCGCCACCATGTGA CGGGCCGGGACGGGC<u>ATG</u>GCCCTGCTGCTGTGCCTGGTGTGCCTGACGGCGCGCGCTGGCCCA

> WO 00/12708 PCT/US99/20111

FIGURE 208

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA76399</pre>

><subunit 1 of 1, 157 aa, 1 stop

><MW: 17681, pI: 7.65, NX(S/T): 1

 ${\tt MALLLCLVCLTAALAHGCLHCHSNFSKKFSFYRHHVNFKSWWVGDIPVSGALLTDWSDDTMK}$ HLAPGSWGGGQLSREGPSLAPEGSMPSPRGDLP ELHLAI PAKI TREKLDQVATAVYQMMDQLYQGKMYF PGYF PNELRNI FREQVHLI QNAI I ER

Signal peptide:

amino acids 1-15

FIGURE 209

TAATTCAGATTCATCTCCTCCTGATAATGAACAAGGCCTCCCCAGAGTATGAAGAGAACATG GTGCTGCCCAGGAACCCACGTGGCTCACAGATGTCCCAGCTGCCATGGAATTCATTGCTGCC TGGTATGAAAGAAAATGGGAAGGTGATATCATTTTTCAAACTAAAGGAGTCTCAACTGCCAG CACAGATACCAGAAGGCAGCCAAGCTCTTCCAGGGGAAGATTCTCTTTATTCTGGTGGACAG CAACAGCCTCCACATGGTGACAGAGTACAACCCTGTGACTGTGATTGGGTTATTCAACAGCG AATTTAGAGGACGAAGACATTGAAAGCATTGATGCCACCAAATTGAGCCGTTTCATTGAGAT CACACTACAACATCACTGGGAACACCATCTGCCTCTTTCGCCTGGTAGACAATGAACAACTG TAGCATGGTGCAAAAATTCCCAGGCGTGTCATTTGGGATCAGCACTGATTCTGAGGTTCTGA ACTGAGGTGGCTGTCATAGGCTTCTTCCAGGATTTAGAAATACCAGCAGTGCCCATACTCCA CCTCACGTGTGAGCTGCCAGAAGTTGCTGCAGAAGTTGAGAAATCCTCAGATGGTCCTG CCTGAACTCAGCAGAAATAGACCATGTGAAAACTCCATGCTTGGTTAGCATCTCCAACTCCC ATGGTTTTAAACACCTTTGTGAAATTGTCTTTTTGCCAGAAGTTAAAGGCTGTCTCCAAGTC TGAAACTCTACCTTCTTTCATAAGCACATGTCCGTCTCTGACTCAGGATCAAAAACCAAAGG TTGTATACTGCACATGACTTACACACACATAGTTCCTGCTCTTTTAAGGTTACCTAAGGGT CCTCTATGAAAGAGAGGCATTCCTAGAGAAAGATTGTTCCAATTTGTCATTTAATATCAAGT CATACTCTGTAAGCCCATCTGTAACACACCTAGATCAAGGCTTTAAGAGACTCACTGTGATG TICITCCTICTTIAAATTICATATCCTCACTCCCTATCCAATTTCCTTCTTATCGTGCATT ACACACGCGCACACACACACACACAGAGCTTCATTTCCTGTCTTAAAATCTCGTTTTCTC AAGTATCTACTTTATGCAAAGTAAAAGGCACAACTCAAATCTCAGAGACACTAAACAACAA TGAATCAGAAGGAAAGACTCCAAAGGTGGAACTC<u>TGA</u>CTTCTCCTTGGAACTACATATGGCC CTTTGGCAATTTACCAGACTCTAGATGACGAGTGGGATACACTGCCCACAGCAGAAGTTTCC AGCAGGAGCAGGAGAGGGACA<u>ATG</u>GAAGCTGCCCCGTCCAGGTTCATGTTCCTCTTATTTCT TATGTAAATCAACAACCTGCATAATAAATAAAAGGCAATCATGTTATA

> WO 00/12708 PCT/US99/20111

FIGURE 210

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA76401

><MW: 30480, pI: 4.60, NX(S/T): 1 ><subunit 1 of 1, 273 aa, 1 stop

esidatki.srfieinslhmvteynpvtviglfnsviqihlllimnkaspeyeenmhryçkaa FFQDLEIPAVPILHSMVQKFPGVSFGISTDSEVLTHYNITGNTICLFRLVDNEQLNLEDEDI CDGFLSGKLLKENRESEGKTPKVEL KLFQGKILFILVDSGMKENGKVISFFKLKESQLPALAIYQTLDDEWDTLPTAEVSVEHVQNP MEAAPSREMFLLELLTCELAAEVAAEVEKSSDGPGAAQEPTWLTDVPAAMEFIAATEVAVIG

Signal peptide:

amino acids 1-20

Transmembrane domain:

amino acids 143-162

FIGURE 211

gtcacttcattctggacacagttggatcaatactgattaagtagaaaatccaagctttgctt AAATGTGTCATATCAATTTCTGGATTCATAATAGCAAGATTAGCAAAGGATAAATGCCGAAG AATACCCATTGGCTATGCCACTTGAAAACAATTTGAGAAGTTTTTTTGAAGTTTTTCTCACT ggcttaagactgattagtcttagcatttactgtagttggaggatggaggtgctatgatggaa CCTTAATGGAGACAATAGCAGATCCTGTAGTATTTCCAGTAGACATGGCCTTTTAATCTAAG CTCAGCAAGAAACAAAACCAAACTGGACTCTCGTGCAGAAAATGTAGCCCATTACCACATGTAGCCTTGGAGAAGAACGATGACGAGGAAAGATGTGT AAGTCAGAGTCTGTGGTGTATGCGGATATCCGAAAGAAT<u>TAA</u>GAGAATACCTAGAACATATC TCCTCGGAAGTCCCCCTCCGACACTGAGGGTCTTGTAAAGAGTCTGCCTTCTGGATCTCACCACGCCGCACACTTATATGCACAGTTAGACCACTCCCGGCGGACATCACAGTGACAAGATTAAAC AACTCTAAACGGGATTACACTGGCTGCAGTACATCAGAGAGTTTGTCACCAGTTAAGCAGGC CTGTGGTCCTAGGTCTCACTCTGCTCATCAGCATGATTCTGGCTGTCCTCTATAGAAGGAAA TATATCTGTGATGTCAAAAACCCCTCCTGACATCGTTGTCCAGCCTGGACACATTAGGCTCTA ACCTTGACAAGAAAGATGCATCAATCAACATAGAAAATATGCAGTTTATACACAATGGCACC CCAAGGGCAAGTGTACCTTGGGAATTATCCACCATTTAAAGACAGAATCAGCTGGGCTGGAG ATGGTACACAAGGGAAGCTGACCTGCAAGTTCAAGTCTACTAGTACGACTGGCGGGTTGACC GCTCTTGACAGCTGGAGTATCAGCCTTGGAAGTATATACGCCAAAAGAAATCTTCGTGGCAA GEGGTGATTGCAGCCCCAGACAGCCGGCGGCGCTGGCTGGTGGTGGTGCTGGCGGCGCGCGCTTGG GACGCGGCGGCGGCGGCGACTGCAGTGGCTGGACG<u>ATG</u>GCAGCGTCCGCCGGAGCCGGG GGAGAGCCGCGGCTGGGACCGGAGTGGGGAGCGCGGCGTGGAGGTGCCACCCGGCGCGGGTG AGGTCATTTACAATTGGGAGATTTCAGAAACATTCCTTTCACCATCATTTAGAAATGGTTTG TGAAAAGATGGTATGATTCTACATATGTACCCATTGTCTTGCTGTTTTTTGTACTTTTTC acaaaggatatgtataaatattctatttagtcatcctgatatgaggagccagtgttgcatga IGTCGTAGAAAAAGAGAATTTGCCTGTGTTTCCAGTTTGGGTAGTGGTGGGCATAGTTACTG TCAGTCTCCTGGAGCTTCCAGCCAGAGGGGGCCGACACTACTGTGTCGTTTTTCCACTACTC

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FIGURE 212

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA76510

><subunit 1 of 1, 269 aa, 1 stop

><MW: 29082, pI: 9.02, NX(S/T): 3

MAASAGAGAVIAAPDSRRWLWSVLAAALGLITAGVSALEVYTPKEIFVANGTQGKLTCKFKS
TSTTGGLTSVSWSFQPEGADTTVSFFHYSQGQVYLGNYPFFKDRISWAGDLDKXDASINIEN
MQFIHNGTYICDVKNPPDIVVQPGHIRLYVVEKENLPVFPVWVVVGIVTAVVLGLTLLISMI
LAVLYRRKNSKRDYTGCSTSESLSPVKQAPRKSPSDTEGLVKSLPSGSHQGFVIYAQLDHSG
GHHSDKINKSESVVYADIRKN

Signal peptide:

amino acids 1-37

Transmembrane domain:

amino acids 161-183

PCT/US99/20111

FIGURE 213

CCCTAAGATTATTTAAAAATGATCCTTTGTTCTTCAAACCTGGTAGTCAGTTTTTGTATTCA TCATTATGAAAAGGACATAAAAAAGGTGAAAGAAGAAAGCTTATAAAGCCTTGAAGATGA GCCGCCCTGCTCCAGGTGCTTCGCCAGAGCCATCGAGAGCAGCCGCGACCTGCTGCACAGGA TTAACACTATTTTATTAATTAAAAGTCAAATTTTCTTTGTTTCCATTCCAAAATCAACCTGC CAGTGATTTACAATAGAGCAAGG<u>TAA</u>ATGAATACCTTCTGCTGTGTCTAGCTATATCGCATC CTATATGCAGAAAATATTCCATGACTTGGATATGCTGACGACTGTGCAGGAAGAAAACGAGC TCAAGGATGAGGTGGGGGCACCGGGCATAGTGGTTGGAGTTTCTGTAGATGGAAAAGAAGTC TGGCAGGTGGGCTGAGGGGCGCGGGCCCCGCGGCAGTCCCCCGGGCCCCCGACCCTGAGGCG ACTITITGGCTATACCCTACTGGCAGCCATAGTAGAGAGAGCTTCAGGATGTAAATATTTGGA aaagaatgattttgaacaaggcgaattatatttgagagaaaagtttgaaaattcaattgaat **ACTAAATTTAAAACAGAGCAGGAGAATGAAGCCAAATGCCGGAATTCAAAACCTGGCAAGAA** TGAAAGAGAATGTTGCATTTGAGCAAGAAAAAGAAGGCAAAAGTAATGAAAAGAATGATTTT TATGAAGGTGAAAAGGTTTCTGTCACAACAAGATTACTGATTTCCCATTTAAGTGGAATTCG CAGGGAAACTGGATCTTGATATTCCAGTACAACATTATGTTCCCGAAATTCCCCAGAAAAAGAA TATGCGAATTGCTAGCATCAGCAAAAGTCTCACCATGGTTGCTCTTGCCAAATTGTGGGAAG TGGT CAGAAGGTTTAGGTTATGCTGATGTTGAGAACCGTGTACCATGTAAACCAGAGACAGT TCGCCTCTGGCCGAGCGCCACAGGAGCAGTCCCTCGCCCCGTGGTCTCCGCAGACCCCGGC TCTCGGCCACGGCTGGGTCGGGGCTCGGGCTGGGGCTGGCGCTCGGGGTGAAGC GCCGGCTGTGCAGAGACGCC<u>ATG</u>TACCGGCTCCTGTCAGCAGTGACTGCCCGGGCTGCCGCC

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FIGURE 214

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA76522

><subunit 1 of 1, 373 aa, 1 stop

><MM: 41221, pI: 8.54, NX(S/T): 0

MYRILSAVTARAAAPGGLASSCGRRGVHQRAGLPPLGHGWVGGLGLGLGLGLALGVKLAGGLRG
AAPAQSPAAPDPEASPLAEPPQEQSLAPWSPQTPAPPCSRCFARAIESSRDLLHRIKDEVGA
PGIVVGVSVDGKEVWSEGLGYADVENRVPCKPETVMRIASISKSLTMVALAKLWEAGKLDLD
IPVQHYVPEFPEKEYEGEKVSVTTRLLISHLSGIRHYEKDIKKVKEEKAYKALKYMKENVAF
EQEKEGKSNEKNDFTKFKTEQENEAKCRNSKPGKKKNDFEQGELYLREKFENSIESIRLFKN

DPLFFKPGSQFLYSTFGYTLLAAIVERASGCKYLDYMQXIFHDLDMLTTVQEENEPVIYNRAR

Signal peptide:

amino acids 1-19

Transmembrane domain:

amino acids 39-60

FIGURE 215

GAATGGCTGTCCCCATCCTCATGTGGCTGTGTGGAGCTCAGCTGTGTTGTGTGGCAGTTTAT TGAACGTTTTGAAAAGCTACAGCTTCCAGCAGCCAAAAGCAACTGTTGTTTTGGCAAGACGG AGCGCCAGACACCGGGGGCCAGGGTGGGGGTGGGGGTGGGGGTTGGTGGGGGTAGTGGCC TCCTTCTTCGCCAAATACIGGATGTACATCATTCCCGTCGTCCTGTTCCTCATGATGTCAGG GCTGTTCAACACCTCGGTGCAGCTGCAGCCGCCCACCACCAGCCCCAGGCCCTGAGACGGCGG TEGAGTCGCACCTGTCGGACCAGCTGACCCTGCACGTGGATGTGGCCGGCAACGTGGTGGGC GGCCCTGGATGGCCTGGAAGCTGGTGGCTATGTCTCCTTCTTGTCCCTGCGTGCTCCCTGG GCTGGAGCACTCATTTGAGATCGATGACAGTGCCAACTTCCGGAAGCGGGGCTCACTGCTCT GGTGCCCCAGGGGTGGGGGGGAAGGTCGAGAGGGCGAGGCCTGTGGCACGGTGGGGGCTGCT TANACTGTCCCCCAGATCGACACGCAAAAAAAAA TCCTGATGTACAAGCTTGATTGAAATTCACTGCTCACTTGATACGTTATTCAGAAACCCAAG TTTGCTGTGTGCCACCCTCCCTGTAAGTCTATTTAAAAACATCGACGATACATTGAAATGTG GTGTCGGTGGTGACGCACCCCGGGGGCTGCCGGGGCCATGAGGTGGAGGACGTGGACCTGGA CGACTCCGGGATGTGGCAGCCCTGAATGGCCTGTACCGGGTCCGGATCCCAAGGCGACCCGG GGAACCAGCAGGATGGTACCTTGTCCCTGTCACAGCGGCAGCTCAGCGAGGAGGAGCGGGGC TOTTGCTGATGGCGGTAGCAGCGCCCAGTCGAGCCGGGCAGCGGCTGCCGGGCCGGGACT AGGCTGGTGGGAAGAAGCCGAGA<u>TT</u>GGCGGCAGCCAGCGCTGGGGGAACCCCGGCTGCTCCTGC CCTTCATTGAGCGCCTGGAGATGGAACAGGCCCAGAAGGCCAAGAACCCCCCAGGAGCAGAAG

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FIGURE 216

></usr/seqdb2/set/DNA/Dnaseqs.min/ss.DNA76529</pre>

><mu: 28004, p2: 5.80, NX(S/T): 1

MAAASAGATRILLILLIMAVAAPSRARGSGCRAGTGARGAGAEGREGEACGTVGLILEHSFEI

DDSANFRKRGSLLWNQQDGTLSLSQRQLSEEERGRLRDVAALNGLYRVRIPRRFGALDGLEA

GGYVSSFVPACSLVESHLSDQLTLHVDVAGNVVGVSVVTHPGGCRGHEVEDVDLELFNTSVQ

LOPPTTAPGPETAAFIERLEMEQAOKAKNPQEQKSFFAKYWMYIIPVVLFLMMSGAPDTGGQ

GGGGGGGGGGGGGGGCCCVPPSL

Signal peptide:

amino acids 1-24

Transmembrane domain: amino acids 226-243

FIGURE 217

GAGCTGCGGGTACCTTCACCTACTGAGGAGCCCTATGCCCCTGAGCTGTAACCCCACTCCAG GTGGCAGCTGAGGCTGTAGCCAGCTGGATAGGGCTTGGGGGCCTGTAGCGCCCTTTGTGGCTGC GACTGACTTTGTGACTGTCCTGTGGTTTCTCCTGCCATTGCTTTGTGTTTTGGGAGGACATGA GACAAGATAGCTGGGACAGACTCTTGAATTCCAGCTATCCGGGATTGTACAGATCTCTCTGT CTGTCATGGTGATGGCTGTGGCAGTGGTGGGACTCTTCACCGTGGTAAGGCATGATGCT CTGGACACCTGTGCTGGACCCACACGGGGCCCCTCTGGGCATTATCTTCTCCAGCTTCATGG GGCAGCGTGCCTTCTCAAGGACCTGTGCTGGAGGCCTGCGTGCCTCCTGTCGGACCGCCGC CATCCCTCTCCTGGCTGGCAGGGGCCTTGGCCCTTCGAAACTGGGGGGAGAACTATGACC CTCAGCCTTCGAGGCCTGGTATATCCATGAGCACGTGGAACGGCATGACTTCCCTGCTGAGT CAAGACTACTTTGTGCTGCTAGTGGGGCGAGCACTTGGTGGGCTGTCCACAGCCCTGCTCTT GCAAGAATTCTTGTGTGCCTTTCTCCCTGACTTACTCACTATGCTGCTTAACCAAACTCTCT CTCTATAAACTCTACCAGCATTACTACTTCCTGGAAGGTCAAATTGCCCATCCTCTATGTCTG AACTGGACTTCTATCAGGTCTACTTCCTGGCCCCTGGCAGCTGATTGGCTTCAGGCCCCCTAC GGAGCCGGACGTGTCCGGGGGCGTCCCCCGCAGACCGGGCCAGCAGGTCGTCCGGGGGCCCCACC ATAAACACTTTTAAATGATCAAAAAAAAAAA TGGGGGTGATGGACTGGAAAGAAGGTGCCAAAAGTTCCCTCTGTGTTACTCCCATTTAGAAA CCTTGTCCTCCATGACAGTGATCGAAAAACAGGCACTCGGAATATGTTCAGCATTTGCTCTG TGGCTTGTGGATTATACTTTCCCAGCATGAGCTTCCTACGGAGAAAGGTGATCCCTGAGACA CTCTACCAGCCCAGGCCAGGAGAGTCCGGTGGAGTCCTTCATAGCCTTTCTACTTATTGAGI CAGCCAGCCTGCTTGGCTCTTCCCTGTACCGTATCGCCACCTCCAAGAGGTACCACCTTCAG GTGCTGCTGCTGGGCACCATACAAGCTCTATTTGAGAGTGTCATCTTCATCTTTGTCTTCCT TGGCCTTGCCTCTACAGTCCTCTTTGGCCTAGTGGCCTCCTCCCTTGTGGATTGGCTGGGTC GGAGCGCTGCTGGAACCCGAGCCGGAGCCGGAGCCACAGCGGGGAGGGTGGCCTGGCGGCCT

220/270

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FIGURE 218

MLUTAYLAFUGLLASCLGLELSRCRAKPFGRACSNPSFLRFQLDFYQVYFLALAADMLQAPY
LYKLYQHYYFLEGQIAILYVCGLASTULFGLVASSLUDMLGRKNSCULFSLTYSLCCLTKLS
QDYFVLLUGRALGGLSTALLFSAFEAWYIHEHVERHDFPAEMIPATFARAAFWNHVLAVVAG
QDAFEVLASWIGLGPVAPFVAAIPLLALAGALALRNWGENYDRQRAFSRTCAGGLRCLLSDRR
VAAEAVASWIGLGPVAPFVAAIPLLALAGALALRNWGENYDRQRAFSRTCAGGLRCLLSDRR
VLLLGTIQALFESVIFIFVFLWTFVLDPHGAPLGIIFSSFMAASLLGSSLYRIATSKRYHLQ
PMHLLSLAVLIVVFSLFMLTFSTSFGQESPVESFIAFILIELACGLYFPSMSFLRRKVIPET
EQAGVLNWFRVPLHSLACLGLLVLHDSDRKTGTRNWFSICSAVMVMALLAVVGLFTVVRHDA
ELRVPSPTEEPYAPEL

Signal peptide:

amino acids 1-18

Transmembrane domain:

amino acids 41-55, 75-94, 127-143, 191-213, 249-270, 278-299,

314-330, 343-359, 379-394, 410-430

FIGURE 219

CACCTGGCTCCAGCCTCCCCTACCCAGGGTCTCTGCACAGTGACCTTCACAGCAGTTGTTGG GAACCCGAAACAAAAGGAGCTGAAGGCAGGTGGCCTGAGAGCCATCTGTGACCTGTCACACT GCCCCCAAGGGTGTCTCATGCTACAAGAAGAGGCAAGAGACAGGCCCCAGGGCCTTCTGGCTA AAAGGGTTTGGGCGTTGCTAGGCTGAAAGGGAAGCCACACCACTGGCCTTCCCCTTCCCCAGG TGG<u>TAG</u>AAGAGTTTGTCCCACATTCCAGCCATAAGTGACTCTGAGCTGGGAAGGGGAAACCC CCATCCCAGTCAATGTCACCAGCATCCCCACCTTTGAGCTGCTGCAACCGCCCTGGACCTTC CCGAGACGGCTACATGATCCGCCGCTCTCTGGAACAGCATGGGCTGCCATGGGCCATCATTT GTGGAGATGATCCAGGACAGTACCCAGCGCACAGCTGACATCCCCGGCCCTCTTCCTGCTCGG GGACCAGATIGCTCIGGTGGAGAGGGGGGGGTGCTCCTTCCTCTCCAAGACTCGGGTGGTCC CACCTTGTCCCCGCTGAACCTCCAGAGGCCTGCGGGGAACTCAGCAACGGTTTCTTCATCCA CGGCTTCCGTATCCATGATTATTTGTACTTTCAAGTGCTGAGTCCTGGGGACATTCGATACA GTCCCCGGCGCGCGGGCTGTTGTTCTCGTGCTCTGGCTCCCCGCGTGCGTCGCGGCCCA OCGA CGCGCGGGGGGGGGCGAGAGGAAAACGCGGGCCGGGCCGGGCCCGGGCCCTGGAGAAAA AGTGGTTTAAAGAGCTGGTGTTTGGGGACTCAATAAACCCCTCACTGACTTTTTAGCAATAAA AGGAATTTTGCTACTTGGAATTTGGAGATAGCATCTGGGGACAAGTGGAGCCAGGTAGAGGA AGGAGCACGGCGGGCGGCGGTGATCATCTCTGACAACGCAGTTGACAATGACAGCTTCTAC TCTTCACAGCCACACCTGCCAAGGACTTTGGTGGTATCTTTCACACAAGGTATGAGCAGATT

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FIGURE 220

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA76532

><subunit 1 of 1, 188 aa, 1 stop ><MW: 21042, pI: 5.36, NX(S/T): 2

MVPGAAGWCCLVLWLPACVAAHGFRIHDYLYFQVLSPGDIRYIFTATPAKDFGGIFHTRYEQ IIILVPAEPPEACGELSNGFFIQDQIALVERGGCSFLSKTRVVQEHGGRAVIISDNAVDNDSF YVEMIQDSTORTADIPALFLLGRDGYMIRRSLEQHGLPWAIISIPVNVTSIPTFELLQPPWTFW

Signal peptide:

amino acids 1-20

FIGURE 221

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FIGURE 222

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA76538

><subunit 1 of 1, 116 aa, 1 stop
><MW: 12910, pI: 6.41, NX(S/T): 1</pre>

><MW: 12910, pI: 6.41, NX(S/T): 1
MELALLCGLVVMAGVIPIQGGILNLNKMVKQVTGKMPILSYWPYGCHCGLGGRGQPKDATDW

CCQTHDCCYDHLKTQGCGIYKDNNKSSIHCMDLSORYCLMAVFNVIYLENEDSE

Important features of the protein: Signal peptide:

amino acids 1-17

Transmembrane domain:

amino acids 1-24

N-glycosylation site.

amino acids 86-89

N-myristoylation sites.

amino acids 20-25, 45-50

Phospholipase A2 histidine active site. amino acids 63-70

FIGURE 223

GGACCGCTATTTCTATTTTGGGAAGCTTGATGGCCAGATCTCCTCTGCCTACCCCAGCCAAG GCGGGTGTCTGTAGGTCTTCTCCTGGTGAAAAGTGTCCAGGTGAAACTTGGAGACTCCTGGG GGCCCTGGAGGAGGCAAGTATTTCAGCACCACTGAAGACTACGACCATGAAATCACAGGGCT CCATGCTGCTGCTCACGCTTGCCCTCCTGGGGGGCCCCACCTGGGCAGGGAAGATGTAT GGTGCCCGGCACAACCAGACGCCCAGTCACAGGCGAGAGCCCTGGG<u>ATG</u>CACCGGCCAGAGG CTCGCTTCTTCCTGGATGGGGGCCCAGGGGGCCCAGGAGAGTATAAAGGCGATGTGGAG AATAAAGCTTCTGCAGAAAA CTGGTGGTGGCTGATGGTACTGCAGTAACTGAGTCGGGACGCTGAATCTGAATCCACCAATA AGCAAACTCACCCGTGGGTCGC<u>TAG</u>GGTGGGGTATGGGGGCCATCCGAGCTGAGGCCATCTGT TTTGAATGGAATTATCCACTAGAGGAGCCGACCACTGAGCCACCAGTTAATCTCACATACTC AGGGCAGGTGCTGGTGGGCATCTATGGCCAGTATCAACTCCTTGGCATCAAGAGCATTGGC ATCACAAAAGTCTTTGTCGCCTTCCAAGCTTTCCTCCGGGGTATGGTCATGTACACCAGCAA ACGTGAAACTGGGAGCCTTAGGTGGGAATACCCAGGAAGTCACCCTGCAGCCAGGCGAATAC

> WO 00/12708 PCT/US99/20111

FIGURE 224

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA76541

><subunit 1 of 1, 178 aa, 1 stop

><MW: 19600, pI: 5.89, NX(S/T): 1

AYPSQEGQVLVGIYGQYQLLGIKSIGFEWNYPLEEPTTEPPVNLTYSANSPVGR MHRPEAMLLLLTLALLGGPTWAGKMYGPGGGKYFSTTEDYDHEITGLRVSVGLLLVKSVQVK LGDSWDVKLGALGGNTQEVTLQPGEYITKVFVAFQAFLRGMVMYTSKDRYFYFGKLDGQISS

amino acids 1-22 Signal peptide:

FIGURE 225

GAAGCTTTCAGTGGACCCAGTGTTTTCCAGTGTGTCCCGAATCTGCAGCGCCTCAACCTGGA TTCCAACAAGCTCACATTTATTGGTCAAGAGATTTTGGATTCTTGGATATCCCTCAATGACA TCAGTCTTGCTGGGAATATATGGGAATGCAGCAGAAATATTTGCTCCCTTGTAAACTGGCTG ATCAACCCATTGAAATITAAATACCACAATCAATGTGAAGCTTGAACTCCGGTTTAATATAA TACCTATTGTATAAGACCCTTTACTGATTCCATTAATGTCGCATTTGTTTTTAAGATAAAACT GACAGACCATGTCCTGGACCTGGAGCTCCTTACAAAGGCTTGATTTATCAGGCAATGAGATC ATAGCCCCCACTGTCTTACTGACAATGCTTTCTTCTGCCGAACGAGGATGCCCTAAGGGCTG
TAGGTGTGAAGGCAAAATGGTATATTGTGAATCTCAGAAATTACAGGAGAATACCCTCAAGTA CAATACAAAGG<u>ATG</u>GGTTTCAATGTAATTAGGCTACTGAGCGGATCAGCTGTAGCACTGGTT TGCTGCTGAATGGGACGGGACCCTGCACCTATAACAAATCGGGCTCCAGGGAGTGTGAGGTA GACTCCCAGCACCCAGGAATTTTATGTAGATTATAAACCCACCAACACGGAGACCAGCGAGA CTGCAGCAGCGCTCCCTCATGCGAAGGCACAGGAAAAAAGAAAAAGACAGTCCCTAAAAGCAAAT TGACGCCGAGCACATCTCTTTCCATAAAATCATCGCGGGCAGCGTGGCGCTTTTCCTGTCCG GAGAGCAAACCCCCTTTGCCCCCGACGGTGGGAGCCACAGAGCCCCGGCCCAGAGACCGATGC ACATTTACGGTCTAACTCCCTGAGAACCATCCCTGTGCGAATATTCCAAGACTGCCGCAACC CAATTTAAAGGGCTCAACCAGCTCACCTGGCTATACCTTGACCATAACCATATCAGCAATAT ACAGGGGCTGTCATGCAACTGGCCCCTAAGCCAAAGCAAAAGACCTAAGGACGACCTTTGAA CCATGAAGATCCTATTACCTAGGAAGATTTTGATGTTTTGCTGCGAATGCGGTGTTGGGGATT TGGTGACTATCAAGGGAACGCGATGCCCCCCCCCCCTCCCCTCTCCCTCTCACTTTGGTGG <u>IGA</u>ACCATTGTGATAAAAAGAGCTCTTAAAAGCTGGGAAATAAGTGGTGCTTTATTGAACTC TGCTCGTCATCCTGCTGGTTATCTACGTGTCATGGAAGCGGTACCCTGCGAGCATGAAGCAG TTGATCTGGCCAGGGCTCTCCCAAAGCCGACGTTTAAGCCCCAAGCTCCCCAGGCCGAAGCAT AGTAAATGTGATCGATGCAGTGAAGAACTACAGCATCTGTGGCAAAAGTACTACAGAGAGGT AAAAGTTTTAAAGGTCTAAGGGAGAATACAATTATCTGTGCCAGTCCCAAAGAGCTGCAAGG TTTTCCAAGGTTGGTCAGCCTTCAGAACCTTTACTTGCAGTGGAATAAAATCAGTGTCATAG TGGAACTTTTGGACCTGGGATATAACCGGATCCGAAGTTTAGCCAGGAATGTCTTTGCTGGC TATAATCAGCTGCATTCTCTGGGATCTGAACAGTTTCGGGGGCTTGCGGAAGCTGCTGAGTTT TCTCCTATTTTCTTAACAATACCTTCAGACCTGTGACAAATTTACGGAACTTGGATCTGTCC TGACGAAAATGCTTTTAATGGAATACGCAGACTCAAAGAGCTGATTCTTAGTTCÇAATAGAA TATCTGCTGGTTGCTTAGGTTTGTCCCTTCGCTATAACAGCCTTCAAAAAACTTAAGTATAAT CCCAAGGGGTCCAATTTTTCCTTGGGTGTCAGCGAGCCCTGACTCACTACAGTGCAGCTG TAITTGTTCTTGGAGTGTTCTGCGTGGCTGGCAAAGAATAATGTTCCAAAAATCGGTCCATCT TTTTTTTAACCGCCCCCTCCCCACCCCCAAAAAAACTGTAAAGATGCAAAAACGTAATAT CCCCAAATTGCCTGGAAGAATACATCATGTTTTTCGATAAGAAGAAATTGTAGGATCCAGTT gaactgggtgctcatcacgggaactgctgggctatggaatacagatgtggcagctcaggtag GCTGAGCGTGTGCGCGGTACGGGGCTCTCCTGCCTTCTGGGCTCCAACGCAGCTCTGTGGCT

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FIGURE 226

PCT/US99/20111

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA77301

><subunit 1 of 1, 513 aa, 1 stop

><MW: 58266, pI: 9.84, NX(S/T): 4 ·

MGPNVIRLLSGSAVALV IAPTVLLTMLSSAERGCPKGCRCEGKMVYCESOKLQEIPSSISAG
CLGLSLRYNGLKCKLKYNQFKGLNQLTWLYLDHINHISNI DENAFROTRIKLELLISSNRISYF
LINNTERPVINLRNLDLSYNQLHSLGSSEGFRGLKKLLSLHLRSNSLRTIFVRIFODCNNLELL
DLGYNRIRSLARNVFAGMIRLKELHLERINQFSKLNILALFPRLVSLQNIYLQNKKISVIGQTH
SWTWSSLQRLDLSGNEIBAFSGPSVFQCVPNLQRLNLDSNKLTFIGQEILDSWISINDISLA
SWIWSSLQRLDLSGNEIBAFSGPSVFQCVPNLQRLNLDSNKLTFIGQEILDSWISINDISLA
RALPKPTFKPKLJRENTHSSKGLRENTIICASPKELQGVNVIDAVKNVSICGKSTTERFDLA
RALPKPTFKPKLPRPKHESKPLPFTVGATEPGPETDADAEHISFHKIIAGSVALFLSVLVI
LLVIYVSWRKYPASMKQLQCRSLMRRHRKKKRQSLKQMTPSTQEFYVDYKPTNTETSENLLN
GTGPCTYNKSGSRECEV

Important features of the protein:

Signal peptide:

amino acids 1-33

Transmembrane domain:

amino acids 420-442

N-glycosylation sites.

amino acids 126-129, 357-360, 496-499, 504-507

cAMP- and cGMP-dependent protein kinase phosphorylation site.
amino acids 465-468

Tyrosine kinase phosphorylation site.

amino acids 136-142

N-myristoylation sites.

amino acids 11-16, 33-38, 245-250, 332-337, 497-502, 507-512

EIGURE 227

GCATTTATTGCAGCATCATGCTAAGAACCTTCGGCATAGGTATCTGTTCCCATGAGGACTGC GTCCAGAACCAGAACCAGAAAGATAGTATTTGAATGAAGGTGAGGGGAGAGAGTAGGAAAAA AACCAAATTAATGCTTCTCCACTAGTATCCAAACAGGCAACAATTAGGTGCTGGAAGTAGTT TTTAAATAGTAAAGTAGCAGGCTTTTGATGTGTCACTGCTGTATCATACTTTTATGCTACAC GTCTGAGGAAGGACAATTCGACAAAAGAATGGATGTTGGAAAAAAATTTTTGGTCATGGAGATG AAACATCAAATTTAGGAATAGTTATTTCAGTTGTTGGAAATGTCCAGAGATCTATTCATATA $AAAACAACC\underline{TGA}$ TTTTAGGTGTGGATTATCAATTTAAAGTATTAACGACATCTGTAATTCCA ATCCTGTTCCTGCTCCATGTTTTGGCCCTTTAGGCTCCCCACCTCCATATGAAGAAATTGTA GACAGAAGCAGCTGTGAGTCCAACTGTTGGAATTCACCTTCAAACTCAAACCCCTGACCTAT ATTGATTCTCACAGGCGCACCATGGCAGTTTTTGCTGTTGGAGACTTGGACTCTATTTATGG AAATTATAATGACCAACACCCTAATGGCTGGTATATCTGGATCCTCCTGCTGCTGGTTTTGG CAAAAACATCCATCACAGATGACATATGATCTTCAGCTGACAAATTTGTTGAACAAAACAAT CTTTTACAGTAATGAATGTGGCCTCCATAGTCCATAGTGTTTCTCTGGAGCCTCAGGGCTTG AGGAGATTGCTGAAGATATAGAGCACATATAATGCCAACACGGGGAGAAAAGAAATTTTCCC GAAAAGTTTGGAGTTGAAGGGTAAAGGATAAATGAAGAGGAAAAGGAAAAGATTACAAGTCT TCCATCACATTTAGGACTCCACTGCAGTATACAGCACACCATTTTCTGCTTTAAACTCTTTC TGTTTGCCGCTATTCCAGTTGGTGCTCTCGGACCTACCATGCGAAGAAGATGAAATGTGTGT TAAAT<u>ATG</u>TCAAGATCCAGACTTTTCAGTGTCACCTCAGCGATCTCAACGATAGGGATCTTG AGTTCTGAGAAAGAAGGAAATAAACACAGGCACCAAACCACTATCCTAAGTTGACTGTCCTT **MAACATCAATAGATATCTAAAAA** AGAAGTAGCAATGAGACATCTTCAAGTGGCATTTTGGCAGTGGCCATCAGCAGGGGGACAGA CTAGCATGGGGTCCATAAAAATTATTATAATTTAACAATAGCCCAAGCCGAGAATCCAACAT

WO 00/12708 PCT/US99/20111

FIGURE 228

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA77303</pre>

><subunit 1 of 1, 146 aa, 1 stop

><MW: 16116, pI: 4.99, NX(S/T): 0

MSRSRLFSVTSAISTIGILCLPLFQLVLSDLPCEEDEMCVNYNDQHPNGWYIWILLLLVLVA ALLCGAVVLCLQCWLRRPRIDSHRRTMAVFAVGDLDSIYGTEAAVSPTVGIHLQTQTPDLYP VPAPCFGPLGSPPPYBEIVKTT

Signal peptide: amino acids 1-29

Transmembrane domain: amino acids 52-70

TIGURE 229

TAATGTTTTGAAATCATGACCCAAAGAATGTATTGATTTGCACTATCCTTCAGAATAACTGA
AGGTTAATTATTGTATATTTTTAAAAATTACACTTATAAGAGTATAATCTTGAAATGGGTAG
CAGCCACTGTCCATTACCTATCGTAAACATTGGGGCAATTTAATAACAGCACTTAAAATAGTT TGTATTGTTCGTCATTATAATATGCTACCACATGTAGCAATAATTACAATATTTTATTAAAA CTCTATAGTAACTGCTTAAGTGCAGCTAGCTTCTAGATTTAGACTATATAGAATTTAGATAT GTATATAGCACAGGGAACCCTAATCTTGGGTAATTCTAGTATAAAACAAATTATACTTTTAT TTAAAATAAGAACATTTAAAATATAAACTATGAAGATTGACTATCTTTTCAGGAAAAAAGCT CTTTATGAAATTTTGAATTTGTATAACAGATGCATTAGATATTCATTTTATATAATGGCCAC Taggaggaagggactttggagaatggaactcttgaggactttagccaggtgtatataataaa ATGCTATCAGGAAAGCACATTATTTCCATATTTGGGTTAATTTTGCTTTTATTATATTGGTC GIAAACCTCTAATCTTATACTTATTGAAGAATAAAAGATATTTTATGATGAGAGTAACAATA AAGTATTCATGATTTTTCACATACATGAATGTTCATTTAAAAGTTTAATCCTTTGAGTGTCT CTTATTGTACTATATTTTGTTATTCCAATTATGAGCAGAGAAAAGGAAATATAATGTTGAAAA ATTTCTATAACACATTTATTTAAGTATATAACACGTTTTTTGGACAAGTGAAGAATGTTTAA TCATTCTGTCATTTGTTCTCAATAGATGTAACTGTTAGACTACGGCTATTTGAAAAAATGTG CTGTACTATGTCCTTAAAGAGAATTTGGTAACTTGGTTGATGTGGTAAGCAGATAGGTGAGT TCTAATTCTGTACATAAAATTTTAAAGTTATTTGTTTGCTTTCAGGCAAGTCTGTTCAATG AGAGCAATACTTTACAATAAAAGCTCTACACATTTTCAAGGAGTATGCTGGATTCATGGAAC TGCTCCATCCACTGTGGATTATATCCTATGGCAGAAAAGCTTTATAATTGCTGGCTTAGGAC ${\tt CCACAAATAAAAGAACGAATGTCTCGGGCAGTATCAGATAGCAGTTGAAAAATCAÇCTTGTGC}$ TGTTGTGAATGGCTCAGCAGCCAACACCACCAATGGTACTAGTGGGAATTTGGTGCCAGTAA ACACAGTGGATGTCGAGAAACGGTGCTTCTATGGCAGGATATGGGGATCTGAAAAGAACAATT GCTGTCCTTCTGGATGACATTTTGCAACGATTGGTGAAGCTGGAGAACAAAGTTGACTATAT CAATCTCAAGAAAAAATATGTCCCAGAAATTGAGTTTACTGTTGCTTGTATTTGGACTCAAT TGGGGATTGATGTTACTGCACTATACTTTTCAACAACCAAGACATCAAAGCAGTGTCAAGTT ACGTGAGCAAATACTAGACTTAAGCAAAAGATATGTTAAAGCTCTAGCAGAGGAAAATAAGA CCCTCTTCAAAACTCATCTCCTGGGTGACTGAGTTAATAGAGTGGATACAACCTTGCTGAAG GCTCTCGCTGCGTCGCCCCGGCTCAGAAGCTCCGTGGCGGCGGCGACCGTGACGAGAAGCCC TTTGTATAAATCTTTTGTGTTTGAGATCAAGCTGAAATGAAAACACTGAAAAACATGGATTC ACGGCCAGCTCAGTTCTCTTCTACTTTGGGAGAGAGAGAAAGTCAGATGCCCCTTTTAAACT TTCTCCAGCTCGATCTGGAGGCTGCTTCGCCAGTGTGGGACGCAGCTGACGCCCGCTTATTA

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WO 00/12708

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FIGURE 230

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA77648

><subunit 1 of 1, 140 aa, 1 stop

><MW: 15668, pI: 10.14, NX(S/T): 5

ENKNTVDVENGASMAGYADLKRTIAVLLDDILQRLVKLENKVDYIVVNGSAAVITNGTSGNL MFFTISRKNMSQKLSLLLLVFGLIWGLMLLHYTFQQPRHQSSVKLREQILDLSKRYVKALAE VPVTTNKRTNVSGSIR

Signal peptide: Important features of the protein:

amino acids 1-26

EIGURE 231

GTCCCGAGTAACTTATGTTCAATGTGCCAACACCAGTGGGGAGCCCGCAGGCCTATGTGGCA TAAAAGTTGTTGCCTTTTTAACGGAGTGTCACTTTCAACCGGCCTCCCCTACCCCTGCTGC TCTACCCCAGGGCAGCATCTCAGCTTCCGAACCCTGGGCTGTTTCCTTAGTCTTCATTTTA CCGTCACCACAGGAGTTGTGGGCCTAGGAGAGGCTTTGGACCTGGGAGCCACACCTAGGAGC GGGCAGGAGCTGAGGTGTTTTCAGGCCTGAGCTCCCTGCAGGAGCTGGACCTTTCGGGCACC AGGTCTCAGTGTCTGCCTTCACGACGCACAGTCAGGGCCGGGCACTACACGTGGACCTCTCC CTTGGACCTGTCCTCCAACCGGCTGGAGATGGTGAATGAGTCGGTGTTGGCGGGGCCGGGCT GTGGATTGTAGCGGCCTGGGCCCCACATCATGCCGGTGCCCATCCCTCTGGACACAGCCCA **АЛАЛАЛАЛАЛАЛАЛАЛАЛАЛАЛАЛАЛАЛАЛАЛАЛА** ATTGTCCTGGGCCTGTGTTGGGGTGTTGGGGGGAAGCTGGGCATCAGTGGCCACATGGGCATC CGGGGATGGAGACATGTCATTTGTAAAAGCAGAAAAAGGTTGCATTTGTTCACTTTTGTAAT CCTTCTTACCCTCCCAGGAATGCCGTGAAAGGAGACAAGGTCTGCCCGACCCATGTCTATGC TCTGGCTGGGATCTCCAAGGGGCCTCCTGGATTCAGTCCCCACTGGCCCTGAGCACGACAGC CATTTTCGCCTGAGCATCCTCTAGATGCTGCCCCAAGGAGTTGCTGCAGTTCTGGAGCCTCA CCAGCCTAGCCAGTTTCTCACCCTGGGTTGGGGTCCCCCAGCATCCAGACTGGAAACCTACC GTGCGGCATGGGCTAAGTCACTCTGCCCTTCGGAGCCTCTGGAAGCTTAGGGCACATTGGTT GGAGTAGCAGCAGCAGGACAGGCAAGAGCCTCACAAGTGGGACTCTGGGCCTCTGACCAGCT ATAAGCCCCACCCTCCCCGCCTGGGCTCCCCTTGCTGCCCTTGCCTGTTCCCCATTAGCACA ATGACTGGAGCACAGCCTCCTGCCTCCCAGCCCGGACCCAATGCACTTTCTTGTCTCCTCTA ttccctagaaccttaatggtagaaggaattgcaaagaatcaagtccacccttctcatgtgac TCTTTTCTAACATAGCCCTTTCTTTGCCATGAGGCCATGAGGCCCGCTTCATCCTTTTCTAT GTTCAGGTCCACTGGGCTGAGTGTCCCCTTGGGCCCATGGCCCAGTCACTCAGGGGCGAGTT ATCTTG<u>TGA</u>CAAATGGTGTGGCCCAGGGCCACATAACAGACTGCTGTCCTGGGCTGCCTCAG CCAGCCCCAAGGTGCCCCTGCACTGCGTAGACACCCGGGAATCTGCTGCCAGGGGCCCCCACC GGGCCAGGATGTGCGGTGCCGGCGCCTGGTGCGGGAGGGCACCTACCCCCGGAGGCCTGGCT AA CCTGGTGCCCTGCCTGAGGCGCTGCTCCTCCACCTCCCGGCACTGCAGAGCGTCAGCGT TGGCTTCCGTGAGCTACCGGGCCTGCAGGTCCTGGACCTGTCGGGCAACCCCAAÇCTTAACT CTGGGAGGCCTTACACACCTGTCTCTGGCCAGCCTGCAGAGGCTCCCTGAGCTGGCGCCCAG TGCGCTACCTGAGCCTGGATGGGAACCCTC1AGCTGTCATTGGTCCGGGTGCCTTCGCGGGG TCAGAGCCTGAACCTGGCCTGGAACCGGCTCCATGCCGTGCCCAACCTCCGAGACTTGCCCC AGCCGAGAGCTTCACCAGCTCACCCCTGAGCGACGTGAACCTTAGCCACAACCAGCTCCGGG CATGCCGTGGCCCCTGCTGCTGCTGCTGCCGTGAGTGGGGCCCAGACAACCCGGCCATGCT CGCGGCCGGGCCGGGGTGAGCGTGCCGAGGCGGCTGTGGCGCAGGCTTCCAGCCCCCAA AGGGGCTGGCCCACAGAGACCCCCACAGGGCAGTGAGCTCTGTCTTCCCCCCACCTGCCTAGC rgategggaaactgaggccttgagaaggaaaaaaggctaatctaagttcctgcgggcagtggc TCCCCGGGTGCCAATGCGAGGTGGAGACCTTCGGCCTTTTCGACAGCTTCAGCCTGACTCGG

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FIGURE 232

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA77652

><subunit 1 of 1, 353 aa, 1 stop

><MW: 37847, pI: 6.80, NX(S/T): 2

MPWPLLLLLAVSGAQTTRPCFPGCQCEVETFGLFDSFSLTRVDCSGLGPHIMPVPIPLDTAH GQDVRCRRLVREGTYPRRPGSSPKVPLHCVDTRESAARGPTIL GFRELPGLQVLDLSGNPKLNWAGAEVFSGLSSLQELDLSGTNLVPLPEALLLHLPALQSVSV QSLNLAWNRI.HAVPNLRDLPLRYLSLDGNPLAVIGPGAFAGLGGLTHLSLASLQRLPELAPS AESFTSSPLSDVNLSHNQLREVSVSAFTTHSQGRALHVDLSHNLIHRLVPHPTRAGLPAPTI LDLSSNRLEMVNESVLAGPGYTTLAGLDLSHNLLTSISPTAFSRLRYLESLDLSHNGLTALF

amino acids 1-16 Signal peptide:

Transmembrane domains:

amino acids 215-232, 287-304

FIGURE 233

GCACATCTACCTTACAATTACTGACCATCCCCAGTAGACTCCCCAGTCCCATAATTGTGTAT CCARABABABABABABABABA CTTCCAGCCAGGAATCCTACACGGCCAGCATGTATTTCTACAAATAAAGTTTTCTTTGCATA AGGGGGGTTATTCATTTGTATTCAACTAAGGACATATTTACTCATGCTGATGCTCTGTGAGA ATTTTTTACTTGGACATGAAACTTTAAAAAATTCACAGATTATATTTATAACCTGACTAG TGTCTTTATGCATCCCCAATCTTAATTGAGACCATACTTGTATAAGATTTTTGTAATATCTT GTACTAGTCTTGTGCTGGTCACAGTGTATCTTATTTATGCATTACTTGCTTCCTTGCATGAT CAAGAGCTCCAGTCTTCAATACCTGCAGAGGAGGCATGACCCCAAACCACCATCTCTTTACT CTTTGAAAAGCTGGAACCTCAGGCAGCAGTTGTGAAGGCTTTGGGGGGAACTAGACATTCTTC GCCCACATGACATGCCATTGTGGGGAGGAAGCAATGAAGAAATACAGCCAGATTCTGAGTCA GGAAGATCAGCAGCCTCGCCAATTCCTTTCTTACCATCAAGAAGGACCTCCGGCTCTCTCAT GCTAAGACTCTATCTGGACAGGGTATTTAAAAACTACCAGACCCCTGACCATTATACTCTCC AGGAGGACTGAGTCTTTGCAAGACACAAAGCCTGCGAATCGATGCTGCCTCCTGCGCCATTT GATTTTCTGAGATACGGGGCAGTGTGCAAGCCAAAGATGGAAACATTGACATCAGAATCTTA ACTGAAGACACTCAATTTGGGAAGCTGTGTGATCGCCACAAACCTTCAGGAAATACGAAATG TCTAGTCTTGCCTTCAGCCTTCTCTCTGCTGCGTTTTATCTCCTATGGACTCCTTCCACTGG GGGAGGCTTGGCAGTTTTTCTTACTCCTGTGGTCTCCAGATTTCAGGCCTAAGATGAAAGCC CACGACCTGIIGCCACCAACTCGCACTCAGACTCTGAACTCAGACCTGAAATCTTCTCTTCAC GTTCCAGGCCTTACCTGCTGGGCACTAACGGCGGAGCCAGGATGGGGACAGAATAAAGGAGC AAACAAGITTTGACATTTCCCCTGAAATGTCATTCTCTATCTATTCACTGCAAGTGCCTGCT TATTTGAAATTGAACCAATGACTACTTAGGATGGGTTGTGGAATAAGTTTTGATGTGGAATT agcaggtgatgtattttatacagtaaaaaaaaaaaccttgtaaattctagaagagtggct TCIGCIAITGGATATATTAITAGTTAATATATTTATTTATTTTTTGCTAITTAATGTATTT TGCAATGGATGGAGGAGACAGAA<u>TAG</u>GAGGAAAGTGATGCTGCTGAGGAATATTCGAGGT GGACCAGAAGGGTGAGCTACGTTGGCTTTCTGGAAGGGGGAGGCTAT<u>ATG</u>CGTCAATTCCCCA GATGGCGCAGCCACAGCTTCTGTGAGATTCGATTTCTCCCCAGTTCCCCTGTGGGTCTGAGG

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FIGURE 234

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA83500

><subunit 1 of 1, 261 aa, 1 stop

><MW: 29667, pI: 8.76, NX(S/T): 0

QEIRNGFSEIRGSVQAKDGNIDIRILRRTESLQDTKPANRCCLLRHLLRLYLDRVFKNYQTP EIFSSREAWQFFLLLWSPDFRPKMKASSLAFSLLSAAFYLLWTPSTGLKTLNLGSCVIATNL MRQFPKTSFDISPEMSFSIYSLQVPAVPGLTCWALTAE PGWGQNKGATTCATNSHSDSELRP ELDILLOWMEETE DHYTLRKISSLANS?LTIKKDLRLSHAHMTCHCGEEAMKKYSQILSHFEKLEPQAAVVKALG

Important features of the protein:

Signal peptide:

amino acids 1-42

amino acids 192-195, 225-228 cAMP- and cGMP-dependent protein kinase phosphorylation sites.

N-myristoylation sites.

amino acids 42-47, 46-51, 136-141

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FIGURE 235

GGAAGGAAAAAGGAAACTGGAAAGGAAAACCATTGCGATTTCGTGGTGTACATCATGCATTTG TCAAGGTGAAGGATTCATGAGTCTATATAAAGGCTTTTTACCATCTTGGCTGAGAATGACCC TGGTAGCTTCTATTCTGGGAACACCAGCCGATGTCATCAAAAGCAGAATAATGAATCAACCA ATTGAATACACCACTTGAGGACAATATCATGACTCACGGTTTATCAAGTTTATGTTCTGGAC AGAGCAGCACTGGTGAATATGGGAGATTTAACCACTTATGATACAGTGAAACACTACTTGGT CAAAAATCTTAGCTGAAGGAGGAATACGAGGGCTTTGGGCAGGCTGGGTACCCAATATACAA GCTGGTGTTATTGGCCAGTTTTTAGCCAATCCAACTGACCTAGTGAAGGTTCAGATGCAAAT TGTTTGGCAAAAGTGAAGATGAGCATTATCCCCTTTGGAAATCAGTCATTGGAGGGATGATG TTACAGACACGTAGTGTATTCTGGAGGTCGAATGGTCACATATGAACATCTCCGAGAGGTTG GCCCTAGGGATCATTGAAGAGGAAGGCTTTCTAAAGCTTTGGCAAGGAGTGACACCCGCCAT CTCTTGCTCGGTTGGGAGACGGTGCAAGAGAATCTGCCCCCTATAGGGGAATGGTGCGCACA CGAGCTAGCAACCTTTCCCCTGGATCTCACAAAAACTCGACTCCAAAATGCAAGGAGAAGCAG CTGACCCAGAGATGGCCCCGAGCGAGCAAATTCCTACTGTCCGGCTGCGCGGCTACCGTGGC CCGTTATCGTCTTGCGCTACTGCTGA<u>ATG</u>TCCGTCCCGGAGGAGGAGGAGGAGGAGGCTTTTGCCG

> WO 00/12708 PCT/US99/20111

FIGURE 236

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA77568

><subunit 1 of 1, 323 aa, 1 stop

><MW: 36064, pI: 9.33, NX(S/T): 1

RGLWAGWVPNIQRAALVNMGDLTTYDTVKHYLVLNTPLEDNIMTHGLSSLCSGLVASILGTP YPLMKSVIGGMMAGVIGQFLANPTDLVKVQMQMEGKRKLEGKPLRFRGVHHAFAKILAEGGI MSVPEEEERLLPLTQRWPRASKFLLSGCAATVAELATFPLDLTKTRLQMQGEAALARLGDGA RESAPYRGMVRTALCIIEEEGFLKLWQGVTPAIYRHVVYSGGRMVTYEHLREVVFGKSEDEH YEKIREMSGVSPF ADVIKSRIMNQPRDKQGRGLLYKSSTDCLIQAVQGEGFMSLYKGFLPSWLRMTPWSMVFWLT

amino acids 25-38, 130-147, 233-248 Transmembrane domains:

FIGURE 237

AAAAATACAAAAATTAGCCAGGCATGGTGGTGGTGCCTGTAATCCCAGCTACCTGGGAGGC TATAATACAAGACTATATGAATTGGATAATGAGTATCAGTTTTTTATTCCTGAGATTTAGAA TTCATTGGTTTCATGTTGATGTTTGGGTCACTTATTGCTTCCATGTGGATTCTTTTTGGTGC ACTGGAGTGAGAAAAAAATGCTGTGGCATCTGTTGTCGCAGGTATATTGTTTTTTACAGGC GCCTGAAGTCGGCGTCGGGCTTTGAGGAAGCTGGGATACAGCATTTAATGAAAAATTTATGC AAAAATATTTGTTCTTATGTATTGAAGAAGTGTACTTTTATATAATGATTTTTTAAATGCCC TAAAAGGTTTTCAGCAAGTTGTAACTTATTTTGGCCTAAAAATGAGGTTTTTTTGGTAAAGA TCTGATTTCTGAAGATGTACAAAAAAATATAGCTTCATATATCTGGAATGAGCACTGAGCCA CCGATTGCTTGAGGTCAAGTGTTTGAGACCAGCCTGGCCAACATGGCGAAACCCCCATCTACT CTTGATCTACTCCCTGAGCCAGGGTTACATCATCTTGTCATTTTTAGAAGTAACCACTCTTGT TGAGTTTTGAAATAGTTTTATGAAATTTCTTTATTTTTCATTGCATAGACTGTTAATATGTA ACACATTGCCAAATGGAGTAGATTGTACATTAAATGTTTTGTTTTCTTTACATTTTTATGTTC TTCTTAAGTCACATTTTCCCTTTTGTTATATTCTGTTTGTAGATAGGTTTTTTATCTCTCAGT TATTTTTTAGCACTCTGATCTACAAATTTGGAAGAACCGAAGAGCTATGGACC<u>TGA</u>GATCAC ATATGTTACCCAAAATACTGATGTTTATCCGGGACTAGCTGTGTTTTTTCAAAATGCACTTA **AGGTGAGAGGTGATAGCTATGAAAGCGGCTGTTTAGGAAGAACAGGTGCTCGAGTTTGGCTT** "ITAAGAAGTAAAAATEGCAGGCTTCCTAGATAATTTTCGTTGGCCAGAATGTGAATGTATTG AAAGGACTAGTTTGAAAGCTTCTTTTAAAAAGAATTCCTCTAATATGACTTTATGTGAGAA TGAGGCAGGAGAATCGCTTGAACCCCGGGGGGCAGAGGTTGCAGTGAGCTGAGTTTGCGCCCAC CTCTCTGGCTGGGCACGGTGGCTCATGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGG TCACACATGTGGTGTATTTTCCACATTGGCTTTCTTCATGATAAATGCTGTATCCAATGCTC TGGTGGATAATGATTGATGCAGCTGTGGTGTATCCTAAGCCAGAACAGTTGAACCATGCCTT

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FIGURE 238

MAGFIDNERWPECECIDWSERRNAVASVVAGILFFTGWWIMIDAAVVYPKPEQLINHAFHTCG
VFSTLAFFMINAVSNAQVRGDSYESGCLGRTGARVWLFIGFMLMFGSLIASMWILFGAYVTQ
NTDVYPGLAVFFQNALIFFSILIYKFGRTEELWT

Important features:

Signal peptide:

amino acids 1-44

Transmembrane domains:

amino acids 23-42 (type II), 60-80, 97-117, 128-148

FIGURE 239

AGCCTCAGAGGGTCCTTCTGGAACCAGCTGTCTGTGGAGAGAATGGGGTGCTTTCGTCAGG GCAGGGGCTGAGGAGGAGGAGCAGGGGGGGTGCTGCGAAGGTGCTGCAGGTCCTTGCACGC GGAAGTGGGAGCCTCGAGCCCTCGGGTGGAAGCTGACCCCAAGCCACCCTTCACCTGGACAG TTTTTGCTGGTTTTGAAAAAAAAAAAAAAAAAA ACTGCTGACGGCTGCTCCTGAGGAAGGACAAACTGCCCAGACTTGAGCCCAATTAAATTTTA TGTGTCGCGCCTCTCCTCGTCGGAAACAGAACCCTCCCACAGCACATCCTACCCGGAAGACC $\mathtt{A}\mathtt{G}\mathtt{G}\mathtt{G}\mathtt{A}\mathtt{T}\mathtt{G}\mathtt{G}\mathtt{C}\mathtt{T}\mathtt{G}\mathtt{G}\mathtt{A}\mathtt{G}\mathtt{G}\mathtt{G}\mathtt{G}\mathtt{G}\mathtt{T}\mathtt{G}\mathtt{G}\mathtt{C}\mathtt{C}\mathtt{C}\mathtt{G}\mathtt{A}\mathtt{A}\mathtt{G}\mathtt{C}\mathtt{C}\mathtt{A}\mathtt{T}\mathtt{T}\mathtt{T}\mathtt{T}\mathtt{A}\mathtt{G}\mathtt{G}\mathtt{G}\mathtt{T}\mathtt{G}\mathtt{G}\mathtt{C}$ gggagttcctacgcaaaacaactgggcttccgggacagctgggtcttcataggagccaaaga CCTCCTACGACGATCCAGGGACCAAAATGAACGATGAAAGCAGGAAACTCTTCTCTGACTTG AGATGTTATGCACCTAGTGAAATTCCTTAAAGAAATTCCGGGGGGTGCACTGGTGCTGGTGG GCCCTGGTGAATGGAACCACCGGAGCTGTGCTGGGACAGAAGGCATTTGACATGTACTCTGG GCTTTGAAGACCGCATGATCATGAGTCCTGTGAAAAAACAATGTGGGCAGAGGCCTAAACATC AGCCAACTACTTTGCGTTTAAAATCTGCAGTGGGGCCGCCAACGTCGTGGGCCCTACTATGT GCCTCGCCCACCAAGGAGATCCAGGTTAAAAAGTACAAGTGTGGCCTCATCAAGCCCTGCCC ©<u>ATG</u>AGAGTGTCAGGTGTGCTTCGCCTCCTGGCCCTCATCTTTGCCCATAGTCACGACATGGA GGTCAGCTGGGTCAGGGACCTACGGCACCTGCTGGACCACCTCGCCTTCTCCATCGAAGCAG GTGAGGCCACTACCCCTCCAGCAACIYGGGAGGTGGGACTGTCAGAAGCTGGCCCAGGGTTGGT CTGGCGGCCCGCAACACTCCGTCTCACCCTCTGGGCCCACTGCATCTAGAGGAGGGCCGTCT GTTGATGGCAAACTTCCTCAAAGGAGGGGAGAGCCTGCGCAGGGCAGGAGCAGCTGGCCCA

> WO 00/12708 PCT/US99/20111

FIGURE 240

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59814

<subunit 1 of 1, 224 aa, 1 stop</pre>

<MW: 24963, pl: 9.64, NX(S/T): 1

Anyfafki csgaanvvgptmcfedrmimspvknnvgrglnialvngttgavlgqkafdmysg DVMHLVKFLKEIPGGALVLVASYDDPGTKMNDESRKLFSDLGSSYAKQLGFRDSWVFIGAKD MRVSGVLRLLALIFALVTTWMFIRSYMSFSMKTIRLPRWLAASPTKEIQVKKYKCGLIKPCP LRGKSPFEQFLKNSPDTNKYEGWPELLEMEGCM9PKPF

Important features:

Sigmal peptide:

amino acids 1-15

ATP/GTP-binding site motif A (P-loop).

amino acids 184-191

N-glycosylation site

amino acids 107-110

FIGURE 241

TATTTGGAAATTAAAGTTTCTGACTTT GAAGTITGGGATATACCCCCAAAGTCCTCTACCCCCTCACTTTTATGGCCCTTTCCCTAGATA GAATGGACCCAGGCTGTCATTCCAGGAAGAACTGCAGAGCCTTCAGCCTCTCCAAACATGTA GGAAAAGCTTCAGGGGACATTGTTCTCCACAGAAGAGGAGCCCTCTAAGCTTCTGGTACAGA GTCCTGGGCATCCTAATTCAGGTGGGTGAGACTAAGAATATAGCTTATGAACACATTCTGAG GGTGGACTTCCCCGAAAATATGTAGCTGCCCAGCTCCACCTGCACTGGGGTCAGAAAGGATC GACATTTGACCCTGATTTGCCTGCTCTGCAGCCCCACGGATATGACCAGCCTGGCACCGAGC TCACTCCTCCCTCTCTCTCTCTGCCTGTCCTAGTCCTCTAGTCCTCAAATTCCCAGTCCC GAGACTGCAGAGGGAGATAAAGAGAGAGGGGCAAAGAGGCAAGAAGAGATTTGTCCTGGGGAT TACTGCGGGATCTCTCCTTAGGATAAAGAGTTGCTGTTGAAGTTGTATATTTTTTGATCAATA GGAGGAAATGAGGAAATCGCTGTTGTTAATGCAGAGANCAAACTCTGTTTAGTTGCAGGG GCCAGAAACACTGTAGGAGTAGTAAGCAGATGTCCTCCTTCCCCTGGACATCTCTTAGAGAG $\mathtt{AGAGTGTGGTCTTCACCTCAGCACAAGCCACGACTGAGGCA}_{\mathtt{AAA}\mathtt{A}\mathtt{A}\mathtt{TTCCTTCTCAGATACCA}$ CCTTCTCCTGGCTGTTTATTTCATTGCTAGAAAGATTCGGAAGAAGAGGCTGGAAAAACCGAA ACTACCGAGCCCTTCAGCCTCTCAATCAGCGCATGGTCTTTGCTTCTTTCATCCAAGCAGGA TCACTTGCATGAAGTCAGGCATAAAGATCAGAAGACCTCAGTGCCTCCCTTCAACCTAAGAG ATTATGACTCTGATTCCTATGACAGCTTGAGTGAGGCTGCTGAGAGGCCTCAGGGCCTGGCT CCCAGGGGGGTCAGAACACCAGATCAACAGTGAAGCCACATTTGCAGAGCTCCAGATTGTAC CTGCACCCCTTCCTGGGACACT<u>ATG</u>TTGTTCTCCGCCCTCCTGCTGGAGGTGATTTGGATCC CCAGAAACCCATGATACCCTACTGAACACCGAATCCCCTGGAAGCCCCACAGAGACAGAGACA TGGATGTGGATGACTTCCCTTCATGCCTATCAGGAAGCCTCTAAAATGGGGTGTAGGATCTG TGCTACCAGAGTGTGCTCTGGACAGTTTTTTATAGAAGGTCCCAGATTTCAATGGAACAGCT TGGCTGCAGATGGGGGTCAACACTGGACGTATGAGGGCCCACATGGTCAGGACCATTGGCCA

244/276

WO 00/12708 PCT/US99/20111

FIGURE 242

><subunit 1 of 1, 337 aa, 1 stop ></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA62812</pre>

><MW: 37668, pI: 6.27, NX(S/T): 1

KDQKTSVPPFNLRELLPKQLGQYFRYNGSLTTPPCYQSVLWTVFYRRSQISMEQLEKLQCTL MLFSALLLEVIWILAADGGQHWTYEGPHGQDHWPASYPECGNNAQSPIDIQTDSVTFDPDLP **IARKIRKKRLENRKSVVFTSAÇATTEA** fsteeepskllvqnyralqplnqrmyfasfiqagssyttgemlslgvgilvgclclllavyf Inseatfaelhivhydsdsydslseaaerpoglavlgilievgetkniayehilshlhevrh ALQPHGYDQPGTEPLDLHNNGHTVQLSLPSTLYLGGLPRKYVAAQLHLHWGQKGSPGGSEHQ

Important features of the protein:

Signal peptide:

amino acids 1-15

Transmembrane domain:

amino acids 291-310

N-glycosylation site

amino acids 213-216

Eukaryotic-type carbonic anhydrases proteins

amino acids 197-245, 104-140, 22-69

FIGURE 243

CTGTCTTTGAAATATAACATTATGCTGCCTGGATGATATGCATATTAAAACATATTTGGAAA GACACATTGGATAGTCTTAGAAGAAATTAATTCTTAATTTACCTGAAAATATTCTTGAAATT CTGCCTCGAATTTGGTGATACATGTGAATCTTTATCATTGATTATATTATGGAATAGATTGA GGAAGCCACCACAGAATCAGCAAATGGAATTCAG<u>TAA</u>GCTGTTTCAAATTTTTTCAACTAAG CCTGCCCACCAGTCAGGCAGGGGCTAATCCAGATGTCCAGGATGGAAGCCTTCCAGCAGGAG AAAAAAAAAAAAAAAAA TCAGAAAATATGTTCTATGTAGAGAATCCCCAACTTTTAAAAACAATAATTCAATGGATAAAT ACAGATGACGACTTTGCAGTGACCACCCCTGCAGGCATCCAAAGGAGCACACATGCCATCGA GAGCAGGTGTAAATCCTGCCACCCAGGGAACCCCAGGCAGCCGCCTCCCAACTCCCAGTGGC TCAGAGGAATTGCCACAAATCTTCACGAGCCTCATCATCCATTCCTTGTTCCCGGGAGGCAT TGCACCCACATGTGTTACCAATTTTTTGTCACACAACTTGGAGCCCAGGGCACTATCCTAAGC AATGACACCTGGTACCCAGACCCACCCATTGACCCTGGGAGGGTTGAATGTACAACAGCAAC ATACCATTAACACAGATGCTCACACTGGGGCCAGATCTGCATCTGTTAAATCCTGCTGCAGG CGGATCAGGGAACACTACCAAAACCAACAGCAGTCAAATCAGGTCTTTCCTTCTTTAAGTCTG ATCAACTCGG!CATTACCACAGCTCAAACCTGCTTTGGGACTCCCTCCCACAAAACTGGCTC GTGGACCCAAAGGTAGCAATCTGAAAC<u>ATG</u>AGGAGTACGATTCTACTGTTTTGTCTTCTAGG AATTTTTCACCAGAGTAAACTTGAGAAACCAACTGGACCTTGAGTATTGTACATTTTGCCTC

> WO 00/12708 PCT/US99/20111

FIGURE 244

TDDDFAVTTPAGIQRSTHAIEEATTESANGIQ LPQIFTSLIIHSLFPGGILPTSQAGANPDVQDGSLPAGGAGVNPATQGTPAGRLPTPSG LTLGPDLHLLNTAAGMTPGTQTHPLTLGGLNVQQQLHPHVLPTFVTQLGAQGTTLSSEE MRSTILLFCLLGSTRSLPQLKFALGLPPTKLAPDQGTLPNQQQSNQVFPSLSLIPLTQM

Signal peptide: amino acids 1-16

FIGURE 245

GGTTTCAATATTTTTTTTTTAGTTGGTTAGAATACTTTCTTCATAGTCACATTCTCTCAACCTA AATGCTTTAATTTTCATTTGCTACCTCTTTTTTTATTATGCCTTGGAATGGTTCACTTAAAT GGAGATGCTTCTACTGGATGGAATTCAGTTTCTCGCATCATTATTGAAGAACTACCAAAATA GAATTGGTGCTGGATTAGTGGATGTTGCTATCTGGGTTGGCACTTGTTCAGATTACCCAAAA CCCTGAAATGAATTCAACAATTAATATTCATCGCACTTCTTCTGTGGAAGGACTTTGTGAAG TCAGTGGCTCACTTCGGCTAAAATGCAGAAATGCATGCTGTCAGCGTTGGTATTTCACATTC GAGTCCTGGACACCCAACTACAAGCAGTGTTCATGGAGTTCATTGAATTATGGCATAGATCT GGATCCCAGGTCGGGATGGATTCAAAGGAGAAAAGGGGGGAATGTCTGAGGGAAAAGCTTTGAG GCCAGCAGGAGTGCCTGGTCGAGACGGGAGCCCTGGGGGCCAATGTTATTCCGGGTACACCTG CAAAAGGCGCAGCTCCCGCAGAGGGAGGTGGTGGACCTGTATAATGGAATGTGCTTACAAGG GCAGCCGGGAGCCATGCGACCCCACGGCCCCGCCGCCTCCCGGCAGCGGCTCCCGCGGCCTCC CAGCCAGACGCTGACCACGTTCCTCTCCTCCGGTCTCCGCCTCCAGCTCCGCGCTGCCCG GGAGAGAGGCGCGCGGTGAAAAGGCGCATTGATGCAGCCTGCGGCGGCGGCCTCGGAAGCGCGGCG AAAAATTATTTCCAACA TGGGAAAATTGCGGAGTGTACATTTACAAAGATGCGTTCAAATAGTGCTCTAAGAGTTTTGT TGCTGCTGCTGCTGCAGCTGCCCCGCGCGCGTCGAGCGCCTCTGAGATCCCCAAGGGGAAG

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FIGURE 246

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA76393
><subunit 1 of 1, 243 ad, 1 stop</pre>

><MW: 26266, pI: 8.43, NX(S/T): 1

MRPQGPAASPQRLRGLLLLLLLQLPAPSSASEIPKGKQKAQLRQREVVDLYNGMCLQGPAGV PGRDGSPGANVIPGTPGIPGRDGFKGEXGECLRESFFFSWTPNYKQCSWSSLNYGIDLGKIA ECTFTKMRSNSALRVLFSGSLRLXCRNACCQRWYFTFNGAECSGPLPIBAIIYLDQGSPEMN STINIHRTSSVEGLCEGIGAGLVDVAIWVGTCSDYPKGDASTGWNSVSRIIIEELPK

Signal peptide:

amino acids 1-30

Transmembrane domain: amino acids 195-217

FIGURE 247A

YYYYYYYXXXXX XXXXXXXXXXXXXXXX (Length = 15 amino acids)

(Length = 12 amino acids)

% amino acid sequence identity =

Comparison Protein

the PRO polypeptide) = sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of (the number of identically matching amino acid residues between the two polypeptide

5 divided by 15 = 33.3%

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FIGURE 247B

Comparison Protein XXXXXXXXX

XXXXXYYYYYYZZYZ (Length = 15 amino acids) (Length = 10 amino acids)

% amino acid sequence identity =

the PRO polypeptide) = sequences as determined by ALIGN-2) divided by (the total number of amino acid residues of (the number of identically matching amino acid residues between the two polypeptide

5 divided by 10 = 50%

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FIGURE 247C

PRO-DNA

NNNNNNNNNNNN

(Length = 14 nucleotides)

NNNNNNLLLLLLLLLL (Length = 16 nucleotides)

% nucleic acid sequence identity =

Comparison DNA

determined by ALIGN-2) divided by (the total number of nucleotides of the PRO-DNA nucleic (the number of identically matching nucleotides between the two nucleic acid sequences as acid sequence) =

6 divided by 14 = 42.9%

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FIGURE 247D

Comparison DNA PRO-DNA

NNNNLLLVV NNNNNNNNNNN (Length = 12 nucleotides)

(Length = 9 nucleotides)

% nucleic acid sequence identity =

acid sequence) = determined by ALIGN-2) divided by (the total number of nucleotides of the PRO-DNA nucleic (the number of identically matching nucleotides between the two nucleic acid sequences as

4 divided by 12 = 33.3%

FIGURE 248A

```
*C-C increased from 12 to 15
*Z is average of EQ
*B is average of ND
*nutch with stop is _M: stop-stop = 0; J (joker) match = 0
*/
                                                                                                                                      z
                                                                                                                                     /* value of a match with a stop */
```

** A C D E F G H J J K L M N O P Q R S T U V W X Y Z */

** A** (2.0.2.0.0.4.1-1.1.0.1.2.1.0. M 1.0.2.1.1.0.0.6.0.3.1).

** A** (2.0.2.0.0.4.1-1.1.0.1.2.1.0. M 1.0.2.1.1.0.0.6.0.2.7.0.4.1).

** C J G J J J J G L J G

FIGURE 248B

```
struct diag {
int
long
short
struct jr
          char char char char in the test to the tes
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          /*
//heltade <sidio.h>
//heltade <crype.h>
//heltade <crype.h>
//define MAXIMP
//define MAXIMP
//define MAXIMP
//define MAXIMP
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                struct jmp {
short
unsigned short
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          #define DMAT
#define DMIS
#define DINSO
#define DINS1
#define PINS0
#define PINSO
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       at un
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           t path (
int
short
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         A
                                                                                     **mer(Z);
*prog;
*prog;
*prog;
dnax0;
dnax0;
dnax0;
dnax0;
edi,
edi,
edi,
edipps;
gpts, gpy;
len0, len1;
*thm;
offiet;
*pf(Z);
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       spe; /* number of leading spaces */
n[IMPS];/* size of jmp (gap) */
x[IMPS];/* loc of jmp (last elem before gap) */
*calloc(), *malloc(), *index(), *strepy();
*getseq(), *g_calluc();
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              4 8 - 8 0 3 4 1024
4 8 - 8 0 3 4 0 1024
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        EMAXIMP];
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     p:
offset:
jpp:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      /* value of marching bases *;
/* penalty for mismarched bases */
/* penalty for a gap */
/* penalty per residue */
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             /* max jumps in a diag */
/* don't continue to penalize gaps larger than this */
/* max jumps in an path */
/* nave if there's an least MX-1 bases since last jump */
/*
                                                                              'ousput file name */
'e and name: gesteapt) */
'e seq name: gesteapt) */
'p seq: gesteapt) */
'e seq: gesteapt) */
'e heat diag: mot or!
'f intal diag: */
'e set if denal: main) */
'e set if penalising cut gaps */
'e set if penalising cut gaps */
'e set if man score: mot or ',
'e man score: mot or ',
'e heat stice of gaps */
'e man score: mot or ',
'e heats diag name in gap file */
'e heats heats and in gride */
'e heats path for seqs */
'e holds path for seqs */
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     /* score at last jmp */
/* offset of prev block */
/* current jmp index */
/* list of jmps */
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            /* size of jmp (neg for dely) */
/* base no. of jmp in seq x */
/* limits seq to 2^16-1 */
```

FIGURE 248C

/* Needleman-Wunsch alignment program

```
main(ac, av)
int
char
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    #include "nw.h"
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           static _dbval[26] = {
1.14.2.13.0.0.4,11.0.0.12.0.3.15.0.0.0.5,6.8.8,7,9,0,10,0
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         * usage: progs file! file?

where file! and file? are two dra or two protein sequences.

where file! and file? are two dra or two protein sequences.

The sequences can be in upper: or lower-case an may contain ambiguity

Any lines beginning with ';' '>' or '<' are ignored.

Max file targeth is 63535 (limited by unsigned short, in the jump stroot)

Assequence with 1/3 or more or its elements ACGTU its assumed to be DNA

Output is in the file *align.out*
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   The program may create a tmp file in /tmp to bold info about traceback.
Original version developed under BSD 4.3 on a vax 8659
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     namez(0] = av[1];
namez(1] = av[2];
soz(0) = getseq(namez(0), &len();
soz(1) = getseq(namez(1), &len();
soz(1) = getseq(namez(1), &len();
abm = (dna)?_dbval;_bbval;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    prog = av[0];
if (ac != 3) {
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        _pma(26) = {
1.2(1<<<0^*A'))(1<<<(N'-A')), 4, 8, 16, 32, 64,
128, 26, 0.4FFFFFF, 1<<10, 1<<11, 1<<12, 1<<13, 1<<14, 1<<12, 1<<21, 1<<21, 1<<22, 1<<22, 1<<22, 1<<22, 1<<22, 1<<22, 1<<22, 1<<22, 1<<23, 1<<24, 1<<22, 1<<24, 1<<25, 1<<24, 1<<25, 1<<25, 1<<24, 1<<25, 1<<25, 1<<24, 1<<25, 1<<24, 1<<25, 1<<25, 1<<24, 1<<25, 1<<25, 1<<24, 1<<25, 1<<25, 1<<25, 1<<24, 1<<25, 1<<25, 1<<25, 1<<26, 1<<26, 1<<25, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1<<26, 1</26, 1<<26, 1</26, 1</26, 1</26, 1</26, 1</26, 1</26, 1</26, 1</26, 1</26, 1</26, 1</26, 1</26, 1</26
                                                                                                                                               nw();
readjmps();
print();
                                                                                                                                                                                                                                                                                                                                                                                                                                               endgaps = 0;
ofile = "align.out";
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   fprint(saderr, 'assge: %s file! file2\n', prog);
fprint(saderr, 'assge: %s file! file2\n', prog);
fprint(saderr, 'better file! and file2 are two date erwo protein sequences, \n');
fprint(saderr, 'better file2 and he in upper- or lover-ease\n');
fprint(saderr, 'Any lines beginning with ': or '< 'are ignored\n');
fprint(saderr, 'Output is in the file1'slign.out\'\n');
file2\n'.
                                                                                                                             /* fill in the matrix, get the possible jmps */
/* get the actual jmps */
/* prins stats, alignment */
/* unlink any trap files */
                                                                                                                                                                                                                                                                                                                                                                                                                             /* 1 to penalize endgaps */
/* output file */
```

main

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/* do the alignment, return best some: main() 'dha: values in Fisch and Smith, PNAS, 89, 1382-1386, 1983 prot PAM 250 values 'When scores are equal, we prefer mismatches to any gap, prefer new gap to extending an ongoing gap, and prefer a gap in sequ " to a gap in seq y. *px, *py: *ndely, *dely; ndelu, delx; *unp; mis: ins0, ins1; id: ij; *col0, *col1; XX, yy: /* sepa and pirs */ /* keep track of dely */ /* keep track of dely */ /* for swapping rowd, row1 */ /* score for each type */ /* insertion penalties */ /* inpo index */ /* jump index */ /* jump index */ /* index into acqs */ /* index into acqs */

W

dx = (struct diag *)g_calloc(*to get diags*, len0+len1+1, sizeof(struct diag));

mely = (int *)g_calloc(*io get ndely*, leal+1, sizoof(las));

dely = (int *)g_calloc(*io get dely*, leal+1, sizzoof(las));

coll = (int *)g_calloc(*io get dely*, leal+1, sizzoof(las));

coll = (int *)g_calloc(*io get coll*, leal+1, sizzoof(las));

incl = (int *)g_calloc(*io get coll*, leal+1, sizzoof(las));

incl = (idas)? DINSO; PINSO;

insl = (idas)? DINSO; PINSO;

 $\begin{aligned} & \text{smax} = -10000; \\ & \text{if } (\text{endipao}) \left\{ & \text{for } (\text{coll}(0)) = \text{del}y(0) = -\text{incd}, \, yy = 1; \, yy < = \text{len1}; \, yy = +) \left\{ & \text{coll}(yy) = -\text{del}y(yy) = -\text{coll}(yy + 1) \cdot \text{inc1}; \\ & \text{ndel}y(yy) = -yy; & \text{ndel}y(yy) = -yy; \end{aligned}$

for (yy = 1; yy < = len1; yy ++) dely[yy] = -ins0; cos0[0] = 0; /* Waterman Bull Math Biol 84 */

for $(px = seqx[0], xx = 1; xx < = len0; px++, xx++) {$ /* initialize first entry ln col/* fill in match matrix If (endgaps) { if (xx = = 1)else ndeix = xx;coll[0] = delx = col0[0] - insl;col1[0] = delx = -(ins0+ins1);

col1[0] = 0; delx = -ins0; ndelx = 0;

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FIGURE 248D

FIGURE 248E

...W

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FIGURE 248F

..nw

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FIGURE 248G

```
"germat() — (tace back best path, count matches; print()
"F.g. lift(n) — print alignment of described in array p(l; print())
"damphlock() — damp a back of lines with numbers, starts; pr_lift(n)
"mm3() — put out a number line: damphlock()
"mm3() — put out a fine feature, [num1, set, [num1]; damphlock()
"sart() — put a line of starts: damphlock()
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           print() - only routine visible outside this module
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     if ((fx = fopen(offic, "w")) = = 0) {
    fprintf(soberr, "$s; can't write $s\n", prog, offie);
    cleamp(l);
getmat(lx. ly. firstgap, lastgap):
pr_align():
                                                                                                                                                                                                                                                                                                                                                                                                                                                   fpindf(x, '< (first sequence: %s (dength = %d)\n', cane.s(0], ken0);
fpindf(x, '< second sequence: %s (dength = %d)\n', came.s((], ken1);
oden = 60;
i.e. = inch;
by = lant;
                                                                    ix, by, firstgap, lastgap: /* overlap */
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    /* set output line length */
/* output file */
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            /* maximum output linc */
/* space between name or num and seq */
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           print
```

extern _day[26][26]; int olen; FILE *fx;

Ndefine SPC 3
Ndefine P_LINE 256
Ndefine P_SPC 3

/include 'nw.h'

* trace back the best path, count matches FIGURE 248H

getmat(lx, ly, firstgap, lastgap) int lx, ly;

firsigap, lasigap;

/* "core" (minus endgaps) "/
/* leading trailing overlap "/

getmat

nm, i0, i1, siz0, siz1; outx[32];

tet nm, 10, 11, s
char oun;(32);
double pc;
register char *f0, n1;
register char *f0, *p1; i0 = i1 = siz0 = siz1 = 0; p0 = seqx[0] + pp[1].spc; p1 = seqx[1] + pp[0].spc; n0 = pp[1].spc + 1; n1 = pp[0].spc + 1; If (endgaps) ix = (len0 < len1)? len0 : len1;/* pct homology:

"if penalizing endgaps, base is the shorter seq

telse, knock off overhangs and take shorter core

" /* get total matches, score }
else If (siz1) {
 p0++;
 n0++;
 siz1-; else (if (n0++ = npf(),x(i0)) sic0 = ppf(),x(i)+ if (n1++ = npf(),x(i)) six1 = ppf(1),x(i)+ six1 = ppf(1),x(i)+ if (xbm[*p0-'A']&xbm[*p1-'A'])

FIGURE 248I

```
pr_align()
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               static
static
static
static
static
static char
static char
static char
static char

    print alignment of described in struct path pp[]

                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 If (dna)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                fprintf(fx, ", gaps in second sequence: %d", gapy);
If (gapy) {
                                                                                                                                                                            f_{x,x}^{(i)}(f_{x,x}^{(i)} < g_{x}^{(i)}) in first sequence: %d*, gapx); If (g_{x}^{(i)})
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     un; /* matches in core - for checking */
igl2; /* lengths of stripped file names */
igl2; /* jmp index for a path */
igl2; /* jmp index for a path */
igl2; /* output elem number -- for gappin
sigl2; /* output element */
*ps[2]; /* per so current element */
*ps[2]; /* per so current element */
*ps[2]; /* per so mext output data slot */
out[2][*]* LINE]; /* output inte */
*sar[*]* LINE]; /* set by gars[*] */
                                                    nc(i) = 1;
ni(i) = 1;
stz(i) = ij(i) = 0;
ps(i) = scqx(i);
po(i) = out(i);
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    fprintf(fx, "<endgaps not penalized'un");</pre>
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     "\ln < score: %d (Dayhoff PAM 250 matrix, gap penalty = %d + %d per residue)\n", 'smax, PiNSO, PINS1);
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                fprintf(ft,
"in < 20070: %d (match = %d, mismatch = %d, gap penalty = %d + %d per base)in",
smax, IMAT, DMIS, DINSO, DINSI);
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          -(endgaps penalized, left endgap: %d %s%s, right endgap: %d %s%s\n', fratgap, (dna)? "base" , "residue", (fratgap == 1)? " : 's', lasgap, (dna)? "base' : "residue", (lasgap == 1)? " : 's');
                                                                                                                                                                                                                                                                                more:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           /* matches in core — for checking */
/* lengths of stripped file names */
/* imp index for a path */
/* number at start of current line */
/* current clem number — for gapping */
                                                                                                                                                                                                                                                                                                                        /* char count */
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                                                                                                                                                                                                                                                                                                                                                           pr_align
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            ...getmat
```

FIGURE 248J

```
* dump a block of lines, including numbers, stars: pr_align()
*/
for (i = 0; i < 2; i++)
*po(i]~ = '\0';
                                                      register i:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               for (nn = nm = 0, more = 1; more; ) {
    for (i = more = 0; i < 2; i++) {
        /*
                                                                                                                                                                                                                      }

H(++m == olen || imore delt m) {

dumpblock():

for (i = 0; i < 2; i++)

pol() = out();

nn = 0;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 else if (siz[i]) { /" in a gap "/
"nn(i)++ = "-";
siz[i]-;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     if (!*ps(i])
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        HOLE++:
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       * do we have more of this sequence?
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        /* we're putting a seq tement

*/

*po(i) = *px(i);

#(slower(*ps(i));

*px(i) = toupper(*px(i));

po(i) + +;

px(i) + +;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               # (ni(i) -- pp(i).x(i(i))) (
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           continue;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       are we at next gap for this seq?
                                                                                                                                                                                                                                                                                                                                                                                     st(i) = pp(i).n(i)(i)++1;
while (ni(i) == pp(i).n(i)(i))
stz(i) += pp(i).n(i)(i)++1;
                                                                                                                                                                                                                                                                                                                                                                                                                                                      * we need to merge all gaps

* at this location
                                                                                  dumpblock
```

FIGURE 248K

* put out a number line: dumpblock() register char for (i = nc[ix], py = out[ix]; "py; py++, pn++) {
 !! ("py == " | | *py == " ")
 *pn = " "; for (pn = pline, i = 0; $i < lmax + P_SPC$; i + +, pn + +)
* $pn = \cdot \cdot$; If (#10 == 0 | | (i == 1 && nc[iz] |= 1)) { $j = (i < 0)^{n} + i : |$ for (yx = yn; j; j := 10, yx -) $yx = j \% 10 + 0^{n} : |$ If (i < 0) yx = i : |nline[P_LINE]; i. j; *pn, *px, *py; ams(f);

if (==0 && *ou(1))

sars(0;

if (==0 && *ou(1))

furine(0;

if (==0 & & *ou(1))

if (i == 0) /* index in out[] holding seq line */ *pn = '';

...dumpblock

Suma

} 'm = '\0': nc(ix) = i; for (m = nine: 'pn; pn++) (redd) puc('\n', fx); (redd) puc('\n', fx);

putline

static putline(ix) ht

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* put out a line (name, [num], seq, [num]); dumpblock()

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FIGURE 248L

...putline

* put a line of stars (seqs always in out[0], out[1]): dumpblock()
*/ for (px = out[ix]; *px; px++)
(vold) punc(*px&0x7F, fx);
(vold) punc('\n', fx); for (px = names(in), i = 0; *px && *px != *; *px++, i++)
(nr(i) pund(*px, t);
(nr (i < |max+P| SPC; i++))
(*void) pund(* ', th); /* these count from 1:

* ni[] is current element (from 1)

* nc[] is number at start of current line
*/ int i; register char *px;

If (*out() || (*out() == `` && *(po()) == ``) ||

!*out() || (*out() == `` && *(po(1) == `'))

return;

px = sar;

for (i = lmax +P_SPC; i; i-)

*px++ = ''; int i;
register char *p0, *p1, cx, *px;

stars

cbe if (dna &&_ day['p0-'A']['p1-'A'] > 0)

cx = '.';

cbe
cx = '.';

... = cx: ... = cx = ...

} *px++ = '\n'; *px++= '\n';

/*
* strip path or prefix from pn. return len: pr_align()
*/

FIGURE 248M

py = 0; for (px = pr; *px; px++) If (*px == '/') py = px + 1; if (py)
 (void) strcpy(pn, py);
return(strlen(pn));

register char *px, *py;

char *pn; /* file name (may be path) */

stripname

FIGURE 248N

getseq(file, len) chær "file; /" file name */ int "len; /" seq len */ / #include "nw.h" #include < sys/file.h> remove any tmp file if we blow / char *jname = '/imp/homgXXXXXXX'; FILE *fj; * read, return per to seq, set dna, len, maxlen * skip lines starting with ',','<', or '>' * seq in upper or lower case */ " cleanup() -- cleanup any imp file "greate() -- read in set, ate das, ten, marken "greate() -- read in set, ate das, ten, marken "greathe() -- callac() with error observin "teidjimps() -- get the good jimps, from imp file if necessary "teidjimps() -- write a filled array of jimps to a imp file: nw() "teidjimps() -- write a filled array of jimps to a imp file: nw() "teidjimps() -- write a filled array of jimps to a imp file: nw() } den = marge = 0; while (fgeu(line, 1024, fp)) { If (*line == ". | | *line == ".>") continue: continue: for (px = line; *px != "a"; px ++) If (isupper(*px) | | islower(*px)) if (supper(*px) | | islower(*px)) char ine[1024], "pseq; register char "px; "py; int nage, tien; FILE "fp; **F**(j) (vold) unlink(jname); exit(i); If ((pseq = malloc((unsigned)(den+6))) = = 0) { fprint(suderr, *%: malloc() failed to get %d bytes for %4u*, prog, den+6, file); if ((fp = fopen(file,"r")) == 0) { fprintf(stderr,"%s: can't read %s\n", prog. file); cxit(1); $pseq[0] = pseq[1] = pseq[2] = pseq[3] = '\0'$: /* tomp file for jeeps */ /* cleanup imp file */ cleanup getseq

FIGURE 2480

...getseq

py = pseq + 4;
*len = tlen;
rewind(fp);

```
g_calloc(msg, nx, sz)
char *msg;
int nx, sz;
                                                                                                                                                                                                                                                                                                                       * get final jmps from dx[] or tmp file, set pp[], reset dmax: main() */
                                                                                                                                                                                                                                                                                         (cadjimps)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   }
*py ++ = '\0';
*py = '\0';
(void) fclose(fp);
dna = natgc > (fcn/3);
return(psoq +4);
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         if ((px = calloc((unsigned)nx, (unsigned)sz)) == 0) {
    if (*msg) {
                  for (i = i0 = i1 = 0, dmax0 = dmax, xx = len0; : i++) {
while (1) {
                                                                                                                                                                                                               register i, j, xx;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        while (fgets(line, 1024, fp)) {

If (*line == '; || *line == '<' || *linc == '>')
                                                                     continue;

for (px = line; "px != '\n'; px++) {

    if (isupper(*px))
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      *py + + = *px;

dis (f (slower(*px))
*py + + = (oupper(*px));

if (index(*ATGCU' - *(py-1)))

name + +;
                                                                                                                                                                                                                                fd = -1:
stz, 10, 11;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            px, *calloc0;
for (j = dx[dmax].ijmp; j >= 0 && dx[dmax].jp.x(j] >= xx; j-)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                  fprintf(stderr, "%s; g_calloc() failed %s (n=%d, sz=%d)\n", prog, msg, nx, sz); exi(1);
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               /* program, calling routine */
/* number and size of elements */
                                                                                                                                                                                                                                                                                     readjmps
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  g_calloc
```

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FIGURE 248P

...readjmps

```
| else if (siz > 0) { /* gap in first seq */
| pp(01.n(s)] = siz;
| pp(01.x(s)] = xx;
| gupx + = siz;
| gupx + = siz;
| '* ignore MAXGAP when doing endgaps */
| iti = (siz < MAXGAP | | endgaps)? siz : MAXGAP;
| iti = (siz < MAXGAP | | endgaps)? siz : MAXGAP;
| iti = (siz < MAXGAP | | endgaps)? siz : MAXGAP;
| iti = (siz < MAXGAP | | endgaps)? siz : MAXGAP;
| iti = (siz < MAXGAP | | endgaps)? siz : MAXGAP;
| iti = (siz < MAXGAP | | endgaps)? siz : MAXGAP;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            (vold) close(fd);
# (f) {
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                \begin{array}{ll} \mbox{for } (i=0, i0-; j<0; j++, i0-) \{ \\ i=pp(0].n(j):pp(0].n(j)=pp(0].n(i0):pp(0].n(i0)=i; \\ i=pp(0].n(j):pp(0].n(j)=pp(0].n(i0):pp(0].n(i0)=i; \\ \end{array} 
                                                                                                                                                                                                                                                                                                                                                                                                       \begin{aligned} & \text{for } (j=0, i1-;j<1i:j++, i1-) \{ \\ & i=pp(11,n[j]; pp(11,n[j]=pp(11,n[i1]; pp(11,n[i1]=i; \\ & i=pp(11,n[j]; pp(11,n[j]=pp(11,n[i1]; pp(11,n[i1]=i; \\ & i=pp(11,n[i1]; pp(11,n[i1]=i; \\ & i=pp(11,n[i1]; pp(11,n[i1]=i; \\ & i=pp(11,n[i1]; pp(11,n[i1]=i; \\ & i=pp(11,n[i1]; pp(11,n[i1]=i; \\ & i=pp(11,n[i1]=i; \\ & i=pp(11
                                                                                                                                                                                                                                                                                                            R ((q >= 0)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        /* reverse the order of jmps
*/
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    }

# (0 >= 0) {

**six = dx[dcmax], [p.n[j];

**six = dx[dcmax], [p.n[j];

**dcmax + = siz;

**if (six < 0) {

**if (six < 0) {

**oo(11,n(j)] =
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               }

If (i >= IMPS) {

fprint(suderr, *%s: too many gaps in alignment\n', prog);

cleansp(l);
G = 0;
offset = 0;
                                                                                                                        (void) unlink(jname);
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              If (j < 0 && da(dmax).offset && (j) {
        (void) lexek(fd. dd(dmax).offset, (j);
        (void) read(fd. (char *)&da(dmax).jp, sizzof(struct jmp));
        (void) read(fd. (char *)&da(dmax).offset, sizzof(steldmax).offset);
        (void) read(fd. (char *)&da(dmax).offset, sizzof(steldmax).offset);
        (void) read(fd. (char *)&da(dmax).offset);</p>
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         \int_{0}^{\pi} |f(t)|^{2} dt gap in second seq */
\int_{0}^{\pi} |f(t)|^{2} dt = siz;
\int_{0}^{\pi} |f(t)|^{2} dt
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       /* id = xx - yy + leni - !
```

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EIGURE 2480

(30) 60/100,383 (30) 60/099,816 (30) 60/099,815 (30) 60/099,812 (30) 60/099,792 (30) 60/099,741 (30) 60/099,642 (20) 60/101,068 (0,0010101,01 (30) 60/100,849 (30) 60/100,848 (30) 60/100,930 (30) 60/100.915 (30) 60/100,711 (30) 60/100,710 (30) 60/100,684 (30) 60/100,683 (30) 60/100,664 (20) 60/100,662 (20) 60/100,661 (30) 60/100,627 (30) 60/100,584 (30) 60/100,390 (30) 60/100,388 808,660,09 (00) (30) 60/099,763 (30) 60/099,754 (30) 60/101,07 10 Sep/sep 1998 (10.09.1998) 17 Sep/sep 1998 (17.09.1998) 15 Sep/sep 1998 (15.09.1998) 15 Sep/aep 1998 (15.09.1998) 15 Sep/sep 1998 (15.09.1998) 10 Sep/sep 1998 (10.09.1998) 10 Septesp 1998 (10.09.1998) 10 Sep/sep 1998 (10.09.1998) 10 Sep/sep 1998 (10.09.1990) 18 Septerp 1998 (16.09,1998) 17 Sep/sep 1998 (17.09.1998) 17 Sep/sep 1998 (17.09.1998) 17 Sepres 1998 (17.09.1998) 17 Sep/sep 1998 (17.09.1998) 16 Sep/sep 1998 (16.09.1998) 17 Sep/sep 1998 (17.09.1998) 16 Sep/sep 1998 (16.09.1998) 16 Sep/sep 1998 (16.09.1998) 16 Sep/sep 1998 (16.09.1998) 18 Sep/exp 1998 (10.09.1998) 18 Septep 1998 (18.09.1998) 18 Sep/sep 1998 (18.09.1998) 18 Sep/sep 1998 (18.09.1998) 18 Sep/sep 1998 (18.09,1998) 16 Sep/sep 1998 (16.09.1998) S S S (30) 60/101,472 (30) 60/103,395 (30) 60/103,328 (30) 60/103,445 (30) 60/102,687 (30) 60/102,684 (30) 60/102,240 (30) 60/102,207 (30) 60/101,916 (30) 60/101,915 (30) 60/101,743 (30) 60/101,741 (30) 60/101,738 (30) 60/101,475 (30) 60/101 477 (30) 60/101,476 (30) 60/101,475 (30) 60/103,315 (30) 60/103,314 (30) 60/103,258 (30) 60/102,965 (30) 60/102,571 (30) 60/102,570 (30) 60/102,487 (30) 60/102,484 (30) 60/102,331 (30) 60/102,330 (30) 60/102,307 23 Sepisep 1998 (23.09.1998) 24 Sepisep 1998 (34.09.1998) 1 Oct/oct 1998 (01.10.1998) 2 Oct/oct 1998 (02.10.1998) 6 Oct/oct 1998 (06.10.1998) 6 Oct/oct 1998 30 Sepkep 1998 (30.09.1998) 1 Oct/oct 1998 (01.10.1998) 29 Sepřep 1998 (29.09.1998) 14 Sep/sep 1998 (24.09.1998) 34 Sep/sep 1998 (24.09,1998) 23 Sep/sep 1998 (23.09.1998) 23 Sep/sep 1998 (23.09.1998) 23 Septosp 1998 (23.09.1998) 7 Oct/oct 1998 (07.10.1998) 7 Oct/oct 1998 (07.10.1998) 30 Sep/sep 1998 (30.09.1998) 30 Sep/sep 1998 (30.09.1998) 29 Sep/sep 1998 (29.09.1998) 29 Sep/sep 1998 (29.09.1998) 29 Sep/sep 1998 (29.09.1998) 19 Sqr/sep 1998 (29.09.1998) 24 Sep/sep 1991 (24.09,1998) 24 Sep/sep 1998 (24.09.1998) 13 Sep/sep 1998 (23.09.1998) 30 Septep 1998 (30.09.1998) 7 Oculoci 1998 (07.10.1998) 돐 ន ន S (30) 60/104,987 (30) 60/104-257 (30) 60/103,711 (30) 60/103,675 (30) 60/103,678 (30) 60/103,401 (30) 60/103,396 (30) 60/105,266 (30) 60/105,169 (30) 60/105,002 (30) 60/105,000 (30) 60/103/533 (30) 60/106,062 (30) 60/105,882 (30) 60/105,881 (30) 60/103,807 (30) 60/105,694 (30) 60/103,693 (30) 60/105,104 (30) 60/106,023 (30) 60/106,856 (30) 60/106,464 (30) 60/108,500 (30) 60/106,384 (30) 60/106,248 (30) 60/106,172 (30) 60/106,033 (30) 60/106,032 (30) 60/106,030 (30) 60/106,029 20 Oct/oct 1998 (20.10.1998) 8 Oct/oct 1998 (08.10.1998) 8 Oct/oct 1998 (08.10.1998) 27 Oct/oct 1998 (27.10.1998) 22 Oct/vci 1998 (72110.1998) 21 Oct/act 1998 (ZI.10.1998) 20 Oct/oct 1998 (20.10.1998) 20 Oct/oct 1998 (20.10.1998) 14 Oct/oct 1998 (14.10.1998) 30 Oct/oct 1998 (30.10.1998) 29 Oct/oct 1998 (19.19.1994) 29 Oct/oct 1998 (19.10.1998) 19 Oct/oct 1998 (29.10.1998) 28 Oct/oct 1998 (28.10.1998) 27 Oct/oct 1998 (27.10.1998) 27 Oct/oct 1998 (27,10,1998) 27 Oct/oct 1998 (27.10.1998) 26 Oct/oct 1998 (26.10.1998) 26 Oct/oct 1998 (26.10.1998) 22 Oct/oct 1998 (22.10.1998) 8 Oct/oct 1998 (08.10.1998)

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3 Newhor 1998 US
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(17.X.11.2996) US

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18 Nuvhov 1998 US (18.11.1998)

(30) 60/108,ESB

(30) 60/108,779

(30) 60/104,788

(30) 60/108,904

18 Nov/nov 1998 (18.11.1998) 18 Novinov 1998 US (18.11.1998) (30) 60/108,775

(30) 60/108,250 (30) 60/108,849

18 Nowher 1998 (18.11.1998)

(30) 60/107,783 (30) 60/106,934 (30) 60/106,932 (30) 60/106,919

3 Nov/nov 1998 (03.11.1998)

(30) 60/108,348 (30) 60/108,925 (30) 60/108,867 (30) 60/108,807 (20) 60/108,806

17 Nov/mov 1998 (17.11.1998)

17 Newboy 1998 US (17.11.1998)

18 Nov/nov 1998 (18.11.1998) 18 Nov/nov 1998 (18.11.1998)

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3 Nov/nov 1998 (03.11.1598) 3 Nov/nov 1998 (03.11.1598) 3 Nov/nov 1998 (03.11.1596)